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(54) **Resurfacing of rodent antibodies**

Oberflächenumformung von rodenten Antikörpern

Remodelage d'anticorps des rongeurs

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'POSSIBLE PROCEDURE FOR REDUCING THE
IMMUNOGENICITY OF ANTIBODY VARIABLE
DOMAINS WHILE PRESERVING THEIR
LIGAND-BINDING PROPERTIES'

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EP 0 592 106 B1

Description**FIELD OF THE INVENTION**

5 [0001] The present invention relates to the development of prediction rules that can be used to accurately model the variable regions (V-regions) of antibodies. The development of these rules and their application in the predictive molecular restructuring of the surfaces of variable domains of non-human monoclonal antibodies enables changing of the surface, i.e., resurfacing, of these monoclonal antibody V-regions to replicate the surface characteristics found on human antibody V-regions. This method of resurfacing non-human monoclonal antibody V-regions to resemble human antibody V-regions is expected to permit the production of functional altered antibodies, which retain the binding parameters of the original non-human monoclonal antibody, with improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region.

BACKGROUND OF THE INVENTION**General Background of Antibodies**

[0002] Murine monoclonal antibodies are widely used as diagnostic and therapeutic agents in the treatment of human disease. Mice can be readily immunized with foreign antigens to produce a broad spectrum of high affinity antibodies. Invariably, the introduction of murine or other rodent antibodies into humans results in the production of a human anti-mouse antibody (HAMA) response due to the presentation of a foreign protein in the body. The production of HAMA in patients can result from the introduction of foreign antibody in a single dose or from extended use in therapy, for example, for the treatment of cancer. Extended use of murine antibody is generally limited to a term of days or weeks in patients before concerns of anaphylaxis arise. Moreover, once HAMA has developed in a patient, future use of murine antibodies for diagnostic or therapeutic purposes is often precluded for the same reasons.

[0003] Beyond ethical considerations, attempts to produce human monoclonal antibodies have not been highly successful for a number of reasons. The production *in vitro* of human monoclonals rarely results in high affinity antibodies. *In vitro* cultures of human lymphocytes yield a restricted range of antibody responses relative to the broad spectrum of reactive antibodies produced *in vivo* through direct immunization of mice. Additionally, in humans, immune tolerance prevents the successful generation of antibodies to self-antigens. All of these factors have contributed to the search for ways to modify the structures of murine monoclonal antibodies to improve their use in patients. Many investigators have attempted to alter, reshape or humanize murine monoclonal antibodies in an effort to improve the therapeutic application of these molecules in patients.

Strategies of Antibody Humanization

[0004] The earliest reports of the controlled rearrangement of antibody domains to create novel proteins was demonstrated using rabbit and human antibodies as described by Bobrzecka, K. et al. (Bobrzecka, K., Konieczny, L., Laidler, P. and Rybarska, J. (1980), Immunology Letters 2, pp. 151-155) and by Konieczny et al. (Konieczny, L., Bobrzecka, K., Laidler, P. and Rybarska, J. (1981), Haematologia 14 (I), pp. 95-99). In those reports, the protein subunits of antibodies, rabbit Fab fragments and human Fc fragments, were joined through protein disulfide bonds to form new, artificial protein molecules or chimeric antibodies.

[0005] Recombinant DNA technology was used to construct gene fusions between DNA sequences encoding mouse antibody variable light and heavy chain domains and human antibody light chain (LC) and heavy chain (HC) constant domains to permit expression of the first recombinant "near-human" antibody (chimeric antibody) product (Morrison, S.L., Johnson, M.J., Herzenberg, L.A. and Oi, V.T. (1984), Proc. Natl. Acad. Sci. U.S.A. 81, pp. 6851-6855).

[0006] The kinetics and immune response in man to chimeric antibodies has been examined (LoBuglio, A.F., Wheeler, R.H., Trang, J., Haynes, A., Rogers, K., Harvey, E.B., Sun, L., Ghrayeb, J. and Khazaeli, M.B. (1989), Proc. Natl. Acad. Sci. 86, pp. 4220-4224).

[0007] Chimeric antibodies contain a large number of non-human amino acid sequences and are immunogenic in man. The result is the production of human anti-chimera antibodies (HACA) in patients. HACA is directed against the murine V-region and can also be directed against the novel V-region/C-region (constant region) junctions present in recombinant chimeric antibodies.

[0008] To overcome some of the limitations presented by the immunogenicity of chimeric antibodies, the DNA sequences encoding the antigen binding portions or complementarity determining regions (CDR's) of murine monoclonal antibodies have been grafted by molecular means in the DNA sequences encoding the frameworks of human antibody heavy and light chains (Jones, P.T., Dear, P.H., Foote, J., Neuberger, M.S. and Winter, G. (1986), Nature 321, pp. 522-525; Riechmann, L., Clark, M., Waldmann, H. and Winter, G. (1988), Nature 332, pp. 323-327). The expressed

recombinant products called reshaped or humanized antibodies are comprised of the framework of a human antibody light or heavy chain and the antigen recognition portions, CDR's, of a murine monoclonal antibody. Several patent applications have been filed in this area including, for example, European Patent Application, Publication No. 0239400; European Patent Application, Publication Nos. 0438310A1 and 0438310A2; International Patent Publication No. WO 91/09967; and International Patent Publication No. WO 90/07861.

[0009] However, it is questionable whether European Patent Application (EP), Publication No. 0239400 is truly enabling. It is not assured in this patent that the best fit is made to assure proper presentation of the CDR loops at the antibody combining site.

[0010] EP Publication Nos. 0438310A1 and 0438310A2 go a step beyond EP Publication No. 0239400 by protecting the importance of uniquely selected human frameworks for the human light chain (LC) and heavy chain (HC) V-regions. These V-region frameworks should show a high degree of sequence similarity with the frameworks of the murine monoclonal antibody and present the CDR's in the appropriate configuration. However, the criteria for sequence matching are no more sophisticated than simple homology searching of the antibody protein or DNA databases.

[0011] International Patent Publication No. WO 91/09967 attempts a further variation of the method disclosed in EP Publication No. 0239400. In International Patent Publication No. WO 91/09967, homology of the donor sequences and the acceptor framework is not important, rather it discloses that a selected set of residues in the LC and HC are critically important to humanization. The ability to make changes at these positions is the basis of International Patent Publication No. WO 91/09967.

[0012] International Patent Publication No. WO 90/07861 proposes four important criteria for designing humanized antibodies. 1) Homology between human acceptor and non-human donor sequences. 2) Use donor rather than acceptor amino acids where the acceptor amino acid is unusual at that position. 3) Use donor framework amino acids at positions adjacent to the CDR. 4) Use donor amino acids at framework positions where the sidechain atom is within 3×10^{-10} (3 Angstroms) of the CDR in a 3-D model. The first antibody humanized by this method retained less than 1/3 the affinity of the original monoclonal antibody.

[0013] None of the above methods for designing a humanized antibody are predictable due to the questions that surround CDR framework interactions. By replacement of murine framework with human framework, there is no guarantee of identical conformations for CDR's because i) the V_L - V_H interaction is not identical in all V-regions and ii) accurate prediction of the CDR-framework interactions are key to faithful reproduction of the antigen binding contacts.

[0014] The above methods do not offer a general solution to solving the issues surrounding antibody humanization, rather the methods as outlined in each reference above involve a substantial amount of trial and error searching to obtain the desired affinity in the final humanized product. More importantly, there is no guarantee that corrective changes in framework amino acids will leave the reshaped V-regions resembling the surface character of a truly human antibody. Therefore, it can be argued that antibodies humanized by the above methods may be immunogenic in man.

Antigenicity of Antibodies

[0015] The antigenicity/immunogenicity of an antibody, including recombinant reshaped antibody products, introduced into humans can be viewed as a surface phenomenon. In general one can view the immune system as scanning the surface of a protein introduced to the body. If the F_v portion of a humanized antibody 'opens-up' in the circulation then internal residues can be presented to the immune system. On the other hand, if the F_v portion is stable and tightly packed then only the surface residues presented by the V-regions and the interface between the V_L and V_H regions will be 'scanned'.

Surface Reshaping or Resurfacing of Antibodies

[0016] The notion of surface presentation of proteins to the immune system raises the prospect of redesigning murine monoclonal antibodies to resemble human antibodies by humanizing only those amino acids that are accessible at the surface of the V-regions of the recombinant F_v . The resurfacing of murine monoclonal antibodies to reduce their immunogenicity could be beneficial in maintaining the avidity of the original monoclonal antibody in the reshaped version, because the natural framework-CDR interactions are retained. The value of maintaining the integrity of the framework-CDR interactions has been illustrated as summarized below.

[0017] In a recent research report, two different reshaped versions of the rat monoclonal antibody, Campath-9 (anti-human CD4), were generated (Gorman, S.D., Clark, M.R., Routledge, E.G., Cobbold, S.P. and Waldmann, H. (1991), Proc. Natl. Acad. Sci. U.S.A. **88**, pp. 4181-4185). In one version, pV_H NEW/ C_{G1} , the acceptor V_H framework was from the human NEW-based heavy chain, which has 47% identical residues to the Campath-9 V_H . While in the second version, pV_H KOL/ C_{G1} , the acceptor V_H framework was from the human KOL antibody, which has 72% identical residues to Campath-9 V_H . Each reshaped antibody contained the identical V_L domain from the human REI antibody sequence. However, the recombinant product of pV_H KOL/ C_{G1} had an avidity for CD4 that was substantially greater than the

product of pV_HNEW/C_{G1}. The authors proposed a reshaping strategy where human sequences, that are highly homologous to the rodent antibody of interest, are transferred, by in vitro mutagenesis, into the rodent V-region to create a "bestfit" reshaped antibody. This strategy uses the term "bestfit" to describe the modeling process, however, there is no quantitative formula employed to assess "bestfit", and so in effect, the process is subjective. Additionally, there is no resurfacing concept presented in that paper.

[0018] The concept of reducing rodent-derived antibody immunogenicity through the replacement of exposed residues in the antibody framework regions which differ from those of human origin is discussed in a recent paper (Padlan, E.A. (1991), *Molecular Immunology* **28**, pp. 489-498). In that paper, the variable domains of two antibody structures, KOL (human) and J539 (mouse), are examined. The crystal structures of the Fab fragments of these two antibodies have been elucidated to high resolution. The solvent accessibility of the exposed framework residues in the variable domains of these two antibodies were compared to a sequence database of human and murine antibody V-region subgroups. On the basis of his findings, Padlan proposed to reduce the antigenicity of allogeneic variable domains [murine V-regions], through replacement of the exposed residues in the framework regions with residues usually found in human antibodies. In murine sequences with the highest similarity to a given human sequence, the number of changes necessary to "humanize" a murine V-region surface would range from 6-15 amino acid changes per V-region. This reference suggests how to convert one antibody surface into another but no general method is developed. Application of the procedure is provided by two examples, a worst-case and a best-case.

Worst Case:

[0019] Among the representative murine kappa V_L sequences examined for which its autologous V_H has been sequenced, S107V_L has the most residues that need to be replaced to humanize it. S107V_L is most similar to the members of the human subgroup VKIV and JK2. The exposed or partially exposed residues that need to be replaced are those at positions 9, 10, 14, 15, 16, 17, 18, 22, 41, 63, 80, 83, 85, 100 and 106. Murine V-region S107V_H is most similar in its framework to the members of the human subgroup VHIII and JH6. The exposed or partially exposed residues in S107V_H that need to be replaced are those at positions 3, 40, 68, 73, 75, 76, 82b and **89**. A total of 23 residues need to be replaced to humanize the variable domains of S107.

Best Case:

[0020] Among the murine V_H sequences examined for which the autologous V_L has also been sequenced, MOPC21V_H has the least number of residues that need to be replaced to humanize it. MOPC21V_H is most similar in its framework to the members of the human subgroup HIII and JH6. The exposed or partially exposed residues that need to be replaced are those at positions 1, 42, 74, 82a, 84, **89** and 108. MOPC21V_L is most similar in its framework to human subgroup VKIV and JK4. The exposed or partially exposed residues that need to be replaced are those at positions 1, 9, 12, 15, 22, 41, 63, 68, 83 and 85. A total of 17 amino acids need to be replaced to humanize the variable domains of MOPC21.

[0021] Of the light chains in the Best- and Worst-Case examples cited above, S107V_L required changes at 15 positions and MOPC21V_L required changes at 10 positions. Only seven of the changes are common to both of these light chain sequences (see underlined residues). Moreover, of the heavy chain residues that need to be replaced to humanize the respective V-regions, S107V_H required changes at 8 positions and MOPC21V_H required changes at 7 positions. In this instance, only one position is common to both of these heavy chain sequences (see residues in boldface).

[0022] An analysis of S107 V-regions alone would not have led to the prediction of which residues to change in MOPC21. The reason for this is that the surface residues in Padlan's analysis are only determined by reference to the crystal structure analysis of one antibody. In addition, the basis for defining the surface exposure of an amino acid at a particular position on that crystal structure is a continuous gradient of change, e.g., the fractional solvent accessibility values (Padlan, E.A. (1990), *Molecular Immunology* **28**, pp. 489-498) were computed, where: 0 to 0.2 = completely buried, 0.2 to 0.4 = mostly buried, 0.4 to 0.6 = partly buried/partly exposed, 0.6 to 0.8 = mostly exposed, and 0.8 or above = completely exposed. By limiting the analysis of exposed surface residues to a single crystal structure and by superimposing a broad range of solvent accessibility ratios on exposed residues, such a modeling strategy could be expected to have a wide margin of error in its calculations. This model fails to take into account the great majority of structural information available in the database for other antibody crystal structures.

SUMMARY OF THE INVENTION

[0023] Accordingly, it is an object of this invention to provide humanized rodent antibodies or fragments thereof, and in particular, humanized rodent monoclonal antibodies that have improved therapeutic efficacy in patients due to the presentation of a human surface on the V-region. This and other objects have been attained by providing a method of

producing paired peptides which may or may not be covalently bonded via a disulfide bond or peptide linker, and which comprise humanized heavy and light chains of a rodent antibody variable region, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
- (b) defining for a rodent antibody variable region a set of heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
- (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
- (d) substituting, in the amino acid sequence of said rodent variable region, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
- (e) constructing three-dimensional models of said variable region of said rodent antibody and of said variable region of said rodent antibody resulting from the substituting specified in said step (d);
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent variable region;
- (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
- (h) replacing the set of rodent antibody variable region surface exposed amino acid residues defined in said step (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
- (i) producing said paired peptides,

wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within $5 \times 10^{-10} \text{m}$ (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said variable region to be humanized are identified.

[0024] Also provided is a method of producing a humanized rodent antibody or fragment thereof by resurfacing, said method comprising:

- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
- (b) defining for a rodent antibody or fragment thereof a set of variable region heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
- (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
- (d) substituting, in the amino acid sequence of said rodent antibody or fragment thereof, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
- (e) constructing three-dimensional models of said variable region of said rodent antibody or fragment thereof and of said variable region of said rodent antibody or fragment thereof resulting from the substituting specified in said step (d);
- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof;
- (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
- (h) replacing the set of rodent antibody surface exposed amino acid residues defined in said step (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
- (i) producing said humanized antibody or fragment thereof;

wherein in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least about 98% of said sequence alignment positions and in that in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within $5 \times 10^{-10} \text{m}$ (5 Ångströms) of any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof to be humanized are identified.

[0025] In a preferred embodiment, the rodent antibody or fragment thereof is a murine antibody, and most preferably murine antibody N901.

BRIEF DESCRIPTION OF THE FIGURES

[0026]

Figure 1 shows an algorithm that can be used for constructing a three-dimensional model of the rodent antibody variable region.

Figure 2 is a diagram showing the approach to determine how to humanize a rodent antibody or fragment thereof according to the present invention.

Figures 3A and 3B are plots of relative accessibility of amino acid residues for twelve antibody F_v structures, mapped onto the sequence alignment of these structures. Structures G1b2 (Jeffrey, P.D., Doctor of Philosophy Thesis, University of Oxford, United Kingdom, 1991), D1.3 (Amit, A.G., Mariuzza, R.A., Phillips, S.E.V. and Poljak, R.J. (1986), *Science* **233**, pp. 747-753), 3D6 (Grunow, R., Jahn, S., Porstman, T., Kiessig, T., Steinkeller, H., Steindl, F., Mattanovich, D., Gurtler, L., Deinhardt, F., Katinger, H. and von R., B. (1988), *J. Immunol. Meth.* **106**, pp. 257-265) and 36-71 (5fab) (Rose, D.R., Strong, R.K., Margolis, M.N., Gefter, M.L. and Petsko, G.A. (1990), *Proc. Natl. Acad. Sci. U.S.A.* **87**, pp. 338-342) are not yet present in the Brookhaven database. The other structures used were: 2hfl (Sheriff, S., Silverton, E.W., Padlan, E.A., Cohen, G.H., Smith-Gill, S.J., Finzel, B.C. and Davies, D.R. (1987), *Proc. Natl. Acad. Sci. U.S.A.* **84**, pp. 8075-8079), 3hfm (Padlan, E., Silverton, E., Sheriff, S., Cohen, G., Smith-Gill, S. and Davies, D. (1989), *Proc. Natl. Acad. Sci. U.S.A.* **86**, pp. 5938-5942), 2fbj (Mainhart, C.R., Potter, M. and Feldmann, R.J. (1984), *Mol. Immunol.* **21**, pp. 469-478), 3fab (Saul, F.A., Amzel, L.M. and Poljak, R.J. (1978), *J. Biol. Chem.* **253**, pp. 585-597), 4fab (Herron, J., He, X., Mason, M., Voss, E. and Edmunson, A. (1989), *Proteins: Struct., Funct., Genet.* **5**, pp. 271-280), 2mcp (Segal, D., Padlan, E., Cohen, G., Rudikoff, S., Potter, M. and Davies, D. (1974), *Proc. Natl. Acad. Sci. U.S.A.* **71**, pp. 4298), 2fb4 (Marquart, M., Deisenhofer, J. and Huber, R. (1980), *J. Mol. Biol.* **141**, pp. 369-391), and 1f19 (Lascombe, M., Alzari, P., Boulot, G., Salujian, P., Tougaard, P., Berek, C., Haba, S., Rosen, E., Nisonof, A. and Poljak, R. (1989), *Proc. Natl. Acad. Sci. U.S.A.* **86**, p. 607). These structures are designated by their Brookhaven entry code. The sequence numbering used here is described in Figures 4A and 4B. Figure 3A graphically shows the relative accessibility for the heavy chain and Figure 3B graphically shows the relative accessibility for the light chain.

Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M., Deisenhofer, J. and Huber, R. (1980), *J. Mol. Biol.* **141**, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), *Nucleic Acids Res.* pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), *Proc. Natl. Acad. Sci. U.S.A.* **87**), and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelz, H. and Zachau, H. (1985), *Nucleic Acids Res.* **3**, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), *J. Exp. Med.* **168**, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), *Sequences of Proteins of Immunological Interest*. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to resurface N901 with a given sequence are marked with bars, back-mutations as determined from F_v models are marked with stars. The sequence homology of given sequences to N901 are shown in brackets after each sequence.

Figure 5 is a stereo plot of mean antibody β -barrel, coordinates determined by iterative multiple fitting of eight antibody structures. Strands 7 and 8 comprise the 'take off' positions for CDR H3 and are not included in the fitting of V_L and V_H regions.

Figure 6 is a plot of RMS deviation from the mean of the eight β -sheet strands comprising the framework. The RMS was calculated from structures F19.9, 4-4-20, NEW, FBj, KOL, HyHEL-5, HyHEL-10 and McPC603. N, C α , C atoms are included in the plot. The residues used are shown in the alignment (Table 2). The most disordered residues are all the residues of strand HFR4, the last residue of LFR1, and the first and last residue of HFR2. The nomenclature of the strands is explained in the alignment in Table 2. LFR1 - #1, LFR2 - #2, LFR3 - #3, LFR4 - #4,

HFR1 - #5, HFR2 - #6, HFR3 - #7, HFRS4 - #8.

Figure 7 is a flowchart of the overall modelling protocol known as CAMAL.

Figure 8 is a plot of superimposed loop backbones for models and x-ray structures discussed in Example 2. The loops are positioned after global framework fit. This does not represent the best local least squares fit, but shows how the loops are positioned globally onto the framework.

Figures 9A to 9D are stereo (N,C- α ,C,O) representations of crystal structures and models of D1.3, 3671 and Gloop-2 variable domain and β -barrel strands described in Example 2. Crystal structures are shown with open bonds, model with solid bonds. The difference between the 3D6-H3 in the model and the crystal structure is due to a 5-7° twist in the extended β -sheet conformation of this loop, Figure 9A: D1.3, Figure 9B: 36-71, Figure 9C: Gloop-2, Figure 9D: 3D6.

Figure 10 is a histogram showing the distribution of loop length for CDR H3 loops, data from Kabat et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition).

DETAILED DESCRIPTION OF THE INVENTION

[0027] The existence of specific, yet different, surface patches in murine and human antibodies may be the origin of the inherited immunogenicity of murine antibodies in humans. Statistical analysis of a database of unique human and murine antibody F_v fragments has revealed that certain combinations of residues in exposed surface positions are specific for human and murine sequences. The combinations are not the same in human and murine F_v domains. However, it is possible to define families of surface residues for the two species of antibodies. These families reveal a novel method for the "humanization" or reshaping of murine antibodies. Humanization is the modification of the solvent accessible surface of a non-human antibody or fragment thereof to resemble the surface of a chosen human antibody or fragment thereof such that the modified non-human antibody or fragment thereof exhibits lower immunogenicity when administered to humans. Such a process applies in the present application to antibody variable regions but could equally well apply to any other antibody fragment. The method is considered to be generally applicable to humanization of rodent antibodies.

[0028] According to the present invention, a statistical analysis is presented which is based on accessibility calculated for a range of antibody crystal structures. When this information is applied to an antibody sequence database, it is possible to discriminate between human and murine antibodies at the sequence level purely on the basis of their surface residue profiles.

Rational Resurfacing Approach

[0029] There are several key features of the resurfacing approach of the present invention.

- 1) This method uses as a starting point, construction of a three-dimensional model of a rodent variable region by known methods;
- 2) A large number (e.g., twelve) of antibody F_v or Fab fragment x-ray crystallographic structures are analyzed to produce an unambiguous set of surface exposed amino acid residues that will be positionally identical for a majority (98%) of antibodies. The set is produced by identifying all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander, C. (1983), Biopolymers **22**, pp. 2257-2637) in which explicit atomic radii are used for each atom type to predict sidechain positions as is described below in more detail;
- 3) Using a complete human antibody database, the best set of human heavy and light chain surface exposed amino acid residues is selected on the basis of their closest identity to the set of surface amino acid residues of the murine antibody;
- 4) In order to retain the conformational structure of the CDRs of the rodent antibody, replacement of any human surface exposed amino acid with the original rodent surface exposed amino acid residue is carried out whenever a surface residue is calculated from the three-dimensional model to be within 5 Angstroms of a CDR residue.

[0030] The general resurfacing approach of the present invention is illustrated in Figure 2. The approach can be divided into two stages. In the first, the rodent framework (white) is retained and only the surface residues changed from rodent (dark grey circles) to the closest human pattern (light grey circles). This should remove the antigenicity of the rodent antibody. In the second stage, surface residues within 5x10⁻¹⁰m (5 Angstroms) of the CDRs are replaced with the rodent equivalents in an attempt to retain antigen binding and CDR conformation.

[0031] The method of the present invention is applicable to whole antibodies as well as antibody fragments. Suitable antibody fragments that can be used can readily be determined by the skilled artisan. Examples of some suitable

fragments include a single chain antibody (SCA), an antibody F_v fragment, Fab fragment, Fab_2 fragment, Fab' fragment, or other portion of an antibody comprising the binding site thereof.

[0032] According to the present invention, an important step in the method for determining how to modify a rodent antibody or fragment thereof by resurfacing is to determine the conformational structure of the variable region of the rodent antibody or fragment thereof to be humanized by constructing a three-dimensional model of the rodent antibody variable region. This can be done by known methods such as those described, for example, in Martin et al. (Martin, A. C.R., Cheetham, J.C. and Rees, A.R. (1989), Proc. Natl. Acad. Sci. U.S.A. **86**, pp. 9268-9272; Methods in Enzymology (1991), **203**, pp. 121-152) and as described in detail in Example 2.

[0033] Martin et al. describe an algorithm which is depicted in Figure 1. The algorithm applies to murine and human antibodies equally well. The present inventors therefore expect that, based on sequence similarity between antibodies of different species (Kabat, E.A. Segments of Proteins of Immunological Interest, National Institutes of Health, U.S.A. 1991), the algorithm will work equally well for rat and other rodent antibodies.

[0034] Briefly, the algorithm depicted in Figure 1 can be summarized as follows. The framework region of an antibody to be modelled is selected on the basis of sequence homology and constructed by a least squares fit onto the six conserved strands of the variable region β -barrel. Light and heavy chain complementarity determining regions are constructed using a combination of canonical structures (Chothia, C. and Lesk, A.M. (1987), J. Molec. Bio. **196**, pp. 901-917), database searching and conformational searching. Detailed descriptions of these methods are described in Example 2 herein and in the above two references (Martin et al. 1989 and 1991).

[0035] According to the present invention, another three-dimensional model is also constructed. The other three-dimensional model is of the rodent antibody variable region having human antibody surface amino acid residues substituted therein at particular rodent antibody surface residue positions.

[0036] This other three-dimensional model is constructed by carrying out the series of steps described next.

[0037] The first of the steps is to generate sequence alignments from relative accessibility distributions from x-ray crystallographic structures of a sufficient number of antibody variable region heavy and light chains to give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0038] As used herein, the term "framework" means the antibody variable region from which the complementarity determining regions have been excluded.

[0039] "Complementarity determining regions" means those amino acid sequences corresponding to the following numbering system as defined by Kabat, E.A. (In Sequences of Immunological Interest, N.I.H., U.S.A., 1991).

Light Chain	L1	residues	24-34
Light Chain	L2	residues	50-56
Light Chain	L3	residues	89-97
Heavy Chain	H1	residues	31-358
Heavy Chain	H2	residues	50-58
Heavy Chain	H3	residues	95-102

[0040] A sufficient number of rodent antibody fragments that need to be analyzed in order to produce the set of framework positions of surface exposed amino acid residues can readily be determined by the skilled artisan through routine experimentation using a database of antibody sequences. Thus, this step can be conducted using suitable databases now in existence or later compiled.

[0041] The x-ray crystallographic structures are used to determine relative accessibility distributions of surface exposed amino acid residues. The relative accessibility distributions identify all those residues whose solvent accessibility is above a given cut-off (typically 30%), calculated using a modification of the method of Kabsch and Sander (Kabsch, W. and Sander C. (1983), Biopolymers **22**, pp. 2257-2637) in which explicit atomic radii are used for each atom type.

[0042] The relative accessibility distributions determined from the x-ray crystallographic structures can then be used to generate sequence alignments which give a set of framework positions of surface exposed amino acid residues which is identical in a majority (98%) of the variable regions.

[0043] The set of framework positions of surface exposed amino acid residues for the variable regions of murine antibodies is shown in Table 1, set forth in Example 1, and was produced using the sequence alignments and accessibility distributions shown in Figures 3A and 3B.

[0044] Once a set of framework positions of surface exposed amino acid residues for the variable regions of the rodent antibodies have been generated, the surface exposed residues of the heavy and light chain pair of the rodent antibody, or fragment thereof, to be humanized can be identified using an alignment procedure such as that described in Example 1 and shown in Figures 3A and 3B. This defines a set of surface exposed amino acid residues of a heavy and light chain pair of a rodent antibody or antibody fragment to be humanized.

[0045] Next, a complete human antibody sequence database is used to identify a set of surface exposed amino acid residues from a human antibody variable region that have the closest positional identity to the set of surface exposed amino acid residues of the variable region of the rodent antibody that is to be humanized. The set of surface exposed

amino acid residues from the human antibodies can be separately identified for a heavy chain and for a light chain that are not naturally paired and/or a set can be identified from a natural human heavy and light chain pair, that is, a pair originating from a single B cell or hybridoma clone. Preferably, the set is one from a natural human heavy and light chain pair.

5 [0046] A humanized rodent antibody that gives the appearance of a human antibody is then predicted by substituting the set of surface exposed amino acid residues from the rodent antibody or fragment thereof to be humanized with the set of surface exposed amino acid residues from the human antibody.

[0047] A three-dimensional model can then be constructed from the resulting, fully substituted variable region of the rodent antibody or fragment thereof. The three-dimensional model is constructed using the same known methods
10 mentioned above for constructing a 3-D model of the original rodent antibody or fragment thereof.

[0048] While the antigenicity of this fully "resurfaced" or humanized antibody should be removed, an additional factor to be addressed is the binding affinity or the binding strength of the resurfaced antibody. Changes in the framework of the variable domain introduced through resurfacing can influence the conformation of the CDR loops and therefore antigen binding of the antibody. According to the present invention, this problem is removed by the next step which is
15 to identify, by means of a comparison of both of the above-described three-dimensional models of the rodent antibody variable region, any residues from the set of surface exposed amino acid residues of the variable region heavy and light chain pair of the human antibody identified that are within 5 Angstroms of any atom of any residue of the rodent antibody or antibody fragment complementarity determining regions (CDRs).

[0049] Any residue(s) so identified is then changed back from the human to the original rodent amino acid residue(s).

20 [0050] The results of this method can then be applied to a particular rodent antibody by well known methods. Briefly, genes for the humanized variable heavy and light chain regions are constructed using standard recombinant DNA methods (Sambrook, J., Fritsch, E.F. and Maniatis, T. (1989), Molecular Cloning, Second Edition). For example, a PCR method can be used (Daugherty et al. (1991), Nucleic Acids Research 19, pp. 2471-2476).

[0051] Variable heavy chain or variable light chain gene constructs are subcloned into appropriate expression vec-
25 tors. Suitable expression vectors contain either a human gamma or human kappa constant region gene, a suitable promoter, a sequence coding for a human immunoglobulin leader peptide (for example: met-gly-trp-ser-cys-ile-ile-leu-phe-leu-val-ala-thr-ala-thr (SEQ ID NO:39), Olandi et al. (1989), PNAS 86, pp. 3833-3837), and a drug selectable marker.

[0052] Heavy and light chain expression plasmids can be co-transfected, for example, by electroporation into suitable
30 cells, for example, SP2/0 cells, and selected with an appropriate drug, G418, for example. Screening for intact antibody can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase.

[0053] As another approach, light chain constructs are transfected, for example, by electroporation into suitable cells,
35 for example, SP2/0 cells and selected, for example, in hygromycin. Screening for light chain expression can be accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human kappa chain antibody, and light chains are detected with, for example, goat anti-human antibody conjugated to alkaline phosphatase.

[0054] A light chain producing line is then used as a host to electroporate in the heavy chain construct. The heavy
40 chain plasmid is co-transfected with a plasmid containing the gene coding for another drug marker, for example, neomycin resistance and selected in the presence of the drug G418. Screening for intact antibody is accomplished by ELISA assay. 96-well plates are coated with, for example, goat anti-human Fc and detected with, for example, goat anti-human light chain conjugated to alkaline phosphatase.

EXAMPLE 1 AND COMPARATIVE EXAMPLES

45 [0055] The superiority of the presently claimed method for determining how to modify a rodent antibody or fragment thereof by resurfacing in order to produce a humanized rodent antibody will now be described by reference to the following example and comparative examples which are illustrative and are not meant to limit the present invention.

A) Analysis for Murine Antibodies

50 [0056] In order to determine the positions which are usually accessible on the surface of the F_v domain of murine antibodies, the accessibility was calculated for twelve Fab x-ray crystallographic structures obtained from the Brookhaven database (Bernstein, F., Koetzle, T., Williams, G., Meyer, E., Brice, M., Rodgers, J., Kennard, O., Shimanouchi, T. and Tasumi, M. (1977), J. Mol. Biol. 112, pp. 535-542). The relative accessibility was calculated using
55 the program MC (Pedersen, J. (1991)), which implements a modified version of the DSSP (Kabsch, W. and Sander, C. (1983), Biopolymers 22, pp. 2257-2637) accessibility calculation routine in which explicit atomic radii are specified for every atom. A residue was defined as being surface accessible when the relative accessibility was greater than 30%. The alignment positions of these residues were conserved in all twelve structures (98% identity). Surface acces-

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sible framework positions constitute 40% of the F_v surface area. The remaining surface accessible residues are in the CDRs and in the interdomain C-terminal region. Figures 3A and 3B show a sequence alignment of the twelve crystal structures, the average relative accessibility, and the 30% accessibility cutoff. Figure 3A shows the alignments relative accessibility for the twelve antibody light chains and Figure 3B shows the alignments and relative accessibility for the antibody heavy chains.

[0057] The surface accessible framework positions were mapped onto a database of unique human and mouse F_v sequences (see lists at the end of this Example). The frequency of particular residues in each of these positions is shown in Table 1. Only residue frequencies higher than 5% are listed.

Table 1:

Distribution of accessible residues in murine and human V _H and V _L chain sequences. All of the positions appear to be conserved which leads to the hyphothesis that immunogenecity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.		
Light chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T 87
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5

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Table 1: (continued)

Distribution of accessible residues in murine and human V _H and V _L chain sequences. All of the positions appear to be conserved which leads to the hypothesis that immunogenicity arises from a specific combination of these surface residues. The sequence numbering is explained in Figures 3A and 3B.			
Heavy chain			
Position	Human	Mouse	
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11	
184	S 70 K 9 P 8	K 42 S 37 T 6	
186	K 53 Q 22 R 7 N 5	K 83 Q 7	
187	G 66 S 21 T 5	G 62 S 18 D 10	
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6	
196	S 91	S 76 A 16	
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11	
208	R 46 T 18 K 17 D 6	T 55 R 26 K 8	
209	A 50 P 21 S 13 T 8	S 67 A 14 T 11	
210	E 46 A 18 D 13 S 9 Z 8 V 5	E 88 D 7	
212	T 91	T 53 S 43	
222	G 17 D 11 P 10 Y 9 V N 8	D 67 A 18	

[0058] None of the entire combinations of surface residues in the human sequences are found in the murine sequences and *vice versa* (see lists at the end of this Example). However, the residues in individual positions appear to be conserved (see Table 1). There are few residues which differ significantly between the species; these are at positions 54 and 91 of the L chain and 168 and 216 of the H chain. Of these positions only position 216 is a non conservative (V to Y) mutation. Differences between human and murine antigenicities are therefore believed to arise from the combinations of residues in these positions.

[0059] In order to determine whether the mouse sequences are more distantly related to human F_v sequences than to other mouse F_v sequences, the homology was calculated using a Dayhoff mutation matrix (Dayhoff, M., Barker, W. and Hunt, L. (1983), Meth. Enz. **91**, pp. 524-545). The homology was calculated between all the sequences in a pool of both human and mouse sequence patches made up of the surface accessible residues. The data was then represented as a density map (not shown) in which the sequences are plotted against each other. The density map can be used to discriminate "murine surfaces" from "human surfaces".

B) Reshaping of Antibody N901

[0060] In order to test the resurfacing approach suggested by the above analysis, three humanization experiments were set up. 1) Traditional loop grafting (Verhoeyen, M.E., Saunders, J.A., Broderick, E.L., Eida, S.J. and Badley, R. A. (1991), Disease markers **9**, pp. 3-4) onto a human F_v framework of known structure (KOL). 2) Resurfacing approach using most similar chain. 3) Resurfacing approach using human sequences with most similar surface residues.

[0061] The antibody used was the murine anti-N901 antibody (Griffin et al. (1983), J. Imm. **130**, pp. 2947-2951). The anti-N901 antibody (also referred to herein as the "N901 antibody") is available commercially from Coulter Corporation under the name NKH-1.

[0062] The alignment of the light chain sequences and heavy chain sequences in Figures 4A and 4B, respectively, show the original N901 antibody and the sequences used in each of the three approaches outlined here.

[0063] Figures 4A and 4B show alignments of sequences generated using the three methods of humanization. Sequences are: 1) Original rodent N901. 2+3) KOL (Marquart, M. Deisenhofer, J. and Huber, R. (1980), J. Mol. Biol. **141**, pp. 369-391) and reshaped N901 using KOL surface. 4+5) Most homologous sequences, L(KV2F) (Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513) and H(G36005) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. **87**) and reshaped N901 using these sequences. 6+7) Most homologous with respect to surface residues, L(KV4B) (Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Poehelz, H. and Zachau, H. (1985), Nucleic Acids Res. **3**, pp. 6515-6529) and H(PLO123) (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. **168**, pp. 229-245), and reshaped N901 using these sequences. The numbering is the same as used in the antibody modelling program ABM (ABM is a trademark for commercial software, Oxford Molecular Ltd., Oxford, U.K.), which is based on structural conservation and not sequence homology as used by Padlan et al. (Kabat, E.A., Wu, T.T., Reid-Miller, M., Perry, H.M. and Gottesman, K.S. (1987), Sequences of Proteins

of Immunological Interest. U.S. Department of Health and Human Services, Fourth Edition). The sequence changes which have to be introduced in order to reshape N901 with a given sequence are marked with bars, and back-mutations as determined from F_v models are marked with stars. The sequence homology of a given sequence to N901 is shown in brackets after each sequence.

(1) Classical Humanization

[0064] In classical humanization the rationale is to graft the rodent CDR's onto a framework of known structure, such that CDR-framework interactions can be accurately monitored by homology modelling. The model of the humanized antibody is compared to that of the original rodent antibody, and possible CDR interacting framework residues are back mutated (marked with '*' in alignment) in order to retain the three-dimensional shape of the CDR's. In this example the antibody KOL was used, giving a low homology score of only 77 and 46 in the heavy and light chains respectively.

(2) Most Similar Chain Resurfacing

[0065] A database of nonredundant human antibody sequences was compiled from available protein and nucleotide sequences. A total of 164 H and 129 L chains were sampled.

[0066] Each of the rodent chains, L and H, were then matched and the most similar human sequence found independently (G36005/KV2F) (Schroeder, H. and Wang, J. (1990), Proc. Natl. Acad. Sci. U.S.A. **87**); Klobeck, H., Meindl, A., Combriato, G., Solomon, A. and Zachau, H. (1985), Nucleic Acids Res., pp. 6499-6513). Surface residues, as outlined in Table 1, were then changed in the rodent sequences to match those of the human sequences. Subsequently a model was built of the resurfaced antibody and compared to the model of the original rodent antibody and back mutation of any CDR interacting residues was performed.

(3) Most Similar Surface Replacement According to the Present Invention

[0067] This method is identical to the above method, except that the similarity is calculated only over the surface residues outlined in Table 1 above.

[0068] The same procedure of surface mutation and subsequent back mutation was performed as in the previous methods. In this case the chosen sequences were PLO123/KV4B (Bird, J., Galili, N., Link, M., Sites, D. and Sklar, J. (1988), J. Exp. Med. **168**, pp. 229-245); Klobeck, H., Bronkamp, G., Combriato, G., Mocikat, R., Pohelz, H. and Zachau, H. (1985), Nucleic Acids Res. **3**, pp. 6515-6529).

[0069] The following lists show the surface residue patterns in mouse and human light and heavy chain antibody variable regions. The sequences are ordered on similarity to one another. There are no pattern matches between mouse and human sequences although there are matches within a species.

MOUSE LIGHT CHAIN SURFACE PATCHES

5	1 KVSE\$MOUSE	:KTSLRPGKGSSDYEEK*	(SEQ ID NO: 40)
	2 PL0101	:KTSLRPGKGSSEYEKK*	(SEQ ID NO: 41)
	3 NS1F19L	:QTSLRPDKGSSDHEKK*	(SEQ ID NO: 42)
	4 KV5US\$MOUSE	:QTSLRPDKGSSDQEEK*	(SEQ ID NO: 43)
	5 MUSIGLDD	:QSSLRPDKGSSDQEEK*	(SEQ ID NO: 44)
	6 PL0220	:QTSLRPDKGSSDPEKK*	(SEQ ID NO: 45)
10	7 KV5J\$MOUSE	:QTSLRPDKGSSDPZKK*	(SEQ ID NO: 46)
	8 MUSIGKABB	:QTSLRPDKGSSDPEKT*	(SEQ ID NO: 47)
	9 MUSIGKCLG	:QTSLRADKGSSDQEEK*	(SEQ ID NO: 48)
	10 MUSIGGVJ2	:QTSLRPDKGKSDSEKK*	(SEQ ID NO: 49)
	11 MUSIGKCRN	:QTSLRPARGSSDQEEK*	(SEQ ID NO: 50)
15	12 MUSIGKCLF	:QTSLRPGRGSSDPEKK*	(SEQ ID NO: 51)
	13 MUSIGKACN	:QTSLRPGRGSSDTEKK*	(SEQ ID NO: 52)
	14 MUSIGKABE	:QISLRPGKGSSDSEKK*	(SEQ ID NO: 53)
	15 KV5P\$MOUSE	:QTSLRPGKGSDSDERK*	(SEQ ID NO: 54)
	16 MUSIGKCNK	:ETALRPGKGASDADKK*	(SEQ ID NO: 55)
20	17 KV3D\$MOUSE	:VTALRPGKGASDEDKK*	(SEQ ID NO: 56)
	18 MUSIGKAAW	:VTALRPGKGASDEEKK*	(SEQ ID NO: 57)
	19 KV3G\$MOUSE	:VTALRPGKGASBABKK*	(SEQ ID NO: 58)
	20 KV3E\$MOUSE	:VTALRPGKGASDEDDE*	(SEQ ID NO: 59)
	21 MUSIGKAAZ	:QTSLRPDKGSSDQETT*	(SEQ ID NO: 60)
25	22 MUSIGKCNB	:QNSLTPGKGSSSPEKK*	(SEQ ID NO: 61)
	23 MUSIGKBA	:VTKVRPGKGSDSDDKK*	(SEQ ID NO: 62)
	24 KVSAS\$MOUSE	:VTKVRPGKGSDSDAEKK*	(SEQ ID NO: 63)
	25 MUSIGKV	:VTRVRPGKGSDSDAEKK*	(SEQ ID NO: 64)
	26 MUSIGKCNM	:LTKVRPGKGSDSDSEKK*	(SEQ ID NO: 65)
30	27 MUSIGKCL1	:VTKVRPGKGSDSDSEQK*	(SEQ ID NO: 66)
	28 KVSBS\$MOUSE	:VTKVRPEKGSDSDAEKK*	(SEQ ID NO: 67)
	29 MUSIGKCSA	:VTKVRPEKGSDSDSEKK*	(SEQ ID NO: 68)
	30 MUSIGKCSR	:VTKVSPGKGSDSDAEKK*	(SEQ ID NO: 69)
	31 MUSIGKCSF	:VTKVRSKGGSZDAEKK*	(SEQ ID NO: 70)
	32 MUSIGKAB	:VTSVKPGKGSDSDAEKK*	(SEQ ID NO: 71)
35	33 PL0014	:VSSVKPGKGSDSDAEKK*	(SEQ ID NO: 72)
	34 MUSIGKACU	:VTSAPGKGSDSDAEKK*	(SEQ ID NO: 73)
	35 PS0023	:VSSAPGKGSDSDAEKK*	(SEQ ID NO: 74)
	36 N\$2MCPL	:VTSARPGKGSDSDAEKK*	(SEQ ID NO: 75)
	37 MUSIGKADV	:VSPAIPGKGSDSDAEKK*	(SEQ ID NO: 76)
40	38 MUSIGKCFP	:VTKARPKGSDSDVEIK*	(SEQ ID NO: 77)
	39 MUSIGLDB	:VTLLPPGKGSDSDAEKK*	(SEQ ID NO: 78)
	40 MUSIGKCNZ	:VTLLQPGKGSDSDAEKK*	(SEQ ID NO: 79)
	41 B27887	:VTLLQPGKGSDSDADKK*	(SEQ ID NO: 80)
	42 H28840	:VTLLQPGKGSDSDAEKK*	(SEQ ID NO: 81)
45	43 KV2G\$MOUSE	:VTLLQAGKGSDSDAEKK*	(SEQ ID NO: 82)
	44 C27887	:VTLLQPGEGSDSDAEKK*	(SEQ ID NO: 83)
	45 JL0029	:LTLLQPGNGSDSDAEKK*	(SEQ ID NO: 84)
	46 MUSIGKAEH	:VTLLQPGKGSDSDAEKI*	(SEQ ID NO: 85)
	47 PS0074	:VTLLPQPGQSDSDPEKK*	(SEQ ID NO: 86)
50	48 MUSIGKCHY	:VTLLPQPGKGSDSDAEKK*	(SEQ ID NO: 87)
	49 MUSIGKCNX	:VTLLPQPGKGSDSDAEKK*	(SEQ ID NO: 88)
	50 KV2D\$MOUSE	:VTFLSPGQGSZDAEKK*	(SEQ ID NO: 89)

55

51	MUSIGKADW	: ESSARPGKGDSDAEKK*	(SEQ ID NO: 90)
52	KV2ASMOUSE	: VTLSSPGQGSDAEKK*	(SEQ ID NO: 91)
53	KV1ASMOUSE	: VTTAKPEKGDSDVEKK*	(SEQ ID NO: 92)
54	F30534	: VTTPKPKDGSDSDVEKK*	(SEQ ID NO: 93)
55	MUSIGKCLO	: VTAPRPGKGASSAEKK*	(SEQ ID NO: 94)
56	G27887	: VTAPKPGKGTSSAEKK*	(SEQ ID NO: 95)
57	MUSIGVKV3	: VTTPKPGKGASSAEKK*	(SEQ ID NO: 96)
58	MUSIGKCNA	: VSAPKPGKGASSAEKK*	(SEQ ID NO: 97)
59	S03410	: VTAPRSGKGASSAEKK*	(SEQ ID NO: 98)
60	B32456	: VTAPKSGKGASSAEKK*	(SEQ ID NO: 99)
61	PL0013	: VTAPKPKDGVSSEAEKK*	(SEQ ID NO: 100)
62	MUSIGLAET	: VTAPKSEKGVSSAEKK*	(SEQ ID NO: 101)
63	MUSIGVKV1	: FTAPKPGKGASSAEKK*	(SEQ ID NO: 102)
64	KV6K\$MOUSE	: LTAPKPGRGVSSAEKK*	(SEQ ID NO: 103)
65	G30560	: VTAPKSGKGASSAEKK*	(SEQ ID NO: 104)
66	MUSIGKBO	: VSAPKPGKGGSSAEKK*	(SEQ ID NO: 105)
67	MUSIGKCNB	: VTAPKPRKGASSAEKK*	(SEQ ID NO: 106)
68	H33730	: VTFLSPGQGNSDAELP*	(SEQ ID NO: 107)
69	MUSIGKCP	: VTFLSPGQGNSDDEL*	(SEQ ID NO: 108)
70	KV2C\$MOUSE	: VTLSSPQSGDSDAEKK*	(SEQ ID NO: 109)
71	MUSIGLAV	: VTAPKSSKGGSSAEKK*	(SEQ ID NO: 110)
72	MUSIGKCNH	: QTSPTPGKGSSDPKK*	(SEQ ID NO: 111)
73	KV5R\$MOUSE	: QISLIPGKGSYDDKK*	(SEQ ID NO: 112)
74	KV6E\$MOUSE	: VTALKSGKGASSAEKK*	(SEQ ID NO: 113)
75	MUSIGKCN1	: VTALKSDKGASSGKK*	(SEQ ID NO: 114)
76	MUSIGLDA	: VTPPSPGQGDSSAEKK*	(SEQ ID NO: 115)
77	C26317	: VTPPSPGQGDSSAEKK*	(SEQ ID NO: 116)
78	PS0073	: VTVRKPGRGDSSDPKK*	(SEQ ID NO: 117)
79	A23986	: QTSVRLGQGSDDPKK*	(SEQ ID NO: 118)
80	MUSIGKABW	: KTSLRPWKGSSDSDKK*	(SEQ ID NO: 119)
81	KV5D\$MOUSE	: QTDVTOGQGSQPKK*	(SEQ ID NO: 120)
82	MUSIGZ6L	: QTAVSQGGSSQSEKK*	(SEQ ID NO: 121)
83	MUSIGKCOE	: LTAPRTNRGSSDSEKK*	(SEQ ID NO: 122)
84	MUSIGKCN	: VTAPSSHGSSDTEKK*	(SEQ ID NO: 123)
85	MUSIGLVD	: LLSLSPLKGDSDPKK*	(SEQ ID NO: 124)
86	S06822	: VTAPTPTGAIKTEKL*	(SEQ ID NO: 125)
87	S06821	: VTIPTPTGAIKTEKL*	(SEQ ID NO: 126)
88	MUSIGLAS	: AVSPTPTGAIKTEKL*	(SEQ ID NO: 127)
89	MUSIGLAR	: AVSPTPTGAIKTEKL*	(SEQ ID NO: 128)
90	LV2B\$MOUSE	: AVSPTPTGVKTEKL*	(SEQ ID NO: 129)
91	MUSIGLAN	: AVSPTPTGAIKTEPS*	(SEQ ID NO: 130)

HUMAN LIGHT CHAIN SURFACE PATCHES

5	1 LV4ASHUMAN	:YLPPTPGVIRSTAMKL*	(SEQ ID NO: 131)
	2 LV4BSHUMAN	:YLPPTPGVIRSTAMRL*	(SEQ ID NO: 132)
	3 LV4ESHUMAN	:YLPPTPGLIRSTSMKL*	(SEQ ID NO: 133)
	4 LV4DSHUMAN	:YLPPTPGLIRSTSVKL*	(SEQ ID NO: 134)
	5 LV4CSHUMAN	:YLPPTPGVIRSTAEKL*	(SEQ ID NO: 135)
	6 LV5ASHUMAN	:YLPPTPGVIRSTAGKL*	(SEQ ID NO: 136)
10	7 LV7ASHUMAN	:YLPATPGVVRSSAGML*	(SEQ ID NO: 137)
	8 LV2GSHUMAN	:SLPPSPGKVRSTAERL*	(SEQ ID NO: 138)
	9 LV2ISHUMAN	:SLPPSPGKVRSTANKL*	(SEQ ID NO: 139)
	10 NS2RHE	:SLPPRPGKVRSSSEKL*	(SEQ ID NO: 140)
	11 HUMIGLAN	:SLPPRPGKVRSSSDKL*	(SEQ ID NO: 141)
15	12 LV1ASHUMAN	:SLPPRPGVRSSSEKL*	(SEQ ID NO: 142)
	13 LV1BSHUMAN	:SLPPRPGKVRSSSEQL*	(SEQ ID NO: 143)
	14 LV1PSHUMAN	:SLPPRPGKVRSSSETL*	(SEQ ID NO: 144)
	15 LV1CSHUMAN	:SLPPKPGKIRSSTGKL*	(SEQ ID NO: 145)
	16 A29700	:SLPPKPGRIRSSTGKL*	(SEQ ID NO: 146)
20	17 HUMIGLAM4	:SLPPKPGKIRSSTGQL*	(SEQ ID NO: 147)
	18 LV1DSHUMAN	:SLPPEPGKIRSSTGRL*	(SEQ ID NO: 148)
	19 LV2KSHUMAN	:SLAPSPGKIRSTAEKL*	(SEQ ID NO: 149)
	20 LV1ISHUMAN	:SLPPRPGKIRSSTGNV*	(SEQ ID NO: 150)
	21 LV2ESHUMAN	:SLRPSPGKVRSTAERL*	(SEQ ID NO: 151)
	22 LV2DSHUMAN	:SLRPSPGKVRSTADKL*	(SEQ ID NO: 152)
25	23 LV2CSHUMAN	:SLRPSPGKVRSTAENL*	(SEQ ID NO: 153)
	24 LV2JSHUMAN	:SLRPSPGKVRSAVEKL*	(SEQ ID NO: 154)
	25 LV1ESHUMAN	:SLPPRPGK-RSSAEKL*	(SEQ ID NO: 155)
	26 LV2BSHUMAN	:SLAPSPGKVRSTVERL*	(SEQ ID NO: 156)
	27 NS1MCWW	:SLAPSPDKIRSTPDKL*	(SEQ ID NO: 157)
30	28 LV2HSHUMAN	:SLALSPGKVRSTAERL*	(SEQ ID NO: 158)
	29 NS1MCG2	:SLPLSAGKVRSTAERL*	(SEQ ID NO: 159)
	30 LV2ASHUMAN	:SLAPSPGKVRSTAAYL*	(SEQ ID NO: 160)
	31 S02083	:SLPLTPGLIRSTAEKL*	(SEQ ID NO: 161)
	32 HUMIGLAM2	:SLPLTPRVIRSTAEKL*	(SEQ ID NO: 162)
35	33 LV6CSHUMAN	:FLHPTPGTDSSSTERL*	(SEQ ID NO: 163)
	34 LV6DSHUMAN	:FLHPTPGTDSSSTERL*	(SEQ ID NO: 164)
	35 LV6ESHUMAN	:FLHPTRVTDSSSTERL*	(SEQ ID NO: 165)
	36 LV6BSHUMAN	:LLPPTPGTNSSSNDKL*	(SEQ ID NO: 166)
	37 HUMIGLK3G	:VLPLSPHRIRSEENL*	(SEQ ID NO: 167)
	38 HUMIGLVC	:SLAPSPAKVRSTAERD*	(SEQ ID NO: 168)
40	39 HUMIGVLLS	:VTAPRPGRIRSDPERK*	(SEQ ID NO: 169)
	40 HUMIGKAX	:VTAPRPGRVRSDEPK*	(SEQ ID NO: 170)
	41 E30609	:VTGPRPGRIRSDPERK*	(SEQ ID NO: 171)
	42 KV3BSHUMAN	:VTGPRPGRIRSDPERK*	(SEQ ID NO: 172)
	43 G30607	:VTGPRPGRVRSDEPK*	(SEQ ID NO: 173)
45	44 KV3NSHUMAN	:VTGPRPGRIRSDPERK*	(SEQ ID NO: 174)
	45 KV1HSHUMAN	:VTAPRPGRIRSESERK*	(SEQ ID NO: 175)
	46 KV3KSHUMAN	:VTGPRPGRIRSDPERK*	(SEQ ID NO: 176)
	47 KV3PSHUMAN	:VTVPRPSRIRSESERK*	(SEQ ID NO: 177)
	48 B26555	:VTAPGPGRIRSESERK*	(SEQ ID NO: 178)
50	49 KV1QSHUMAN	:QTSVRPGRVRSDEPK*	(SEQ ID NO: 179)
	50 KV1WSHUMAN	:QTSVRPGRVRSDEPK*	(SEQ ID NO: 180)

51	KV1M\$HUMAN	:QTSVRPGKVRSDPEKK*	(SEQ ID NO: 181)
52	KV1R\$HUMAN	:QTSVRPGKVRSEPEKK*	(SEQ ID NO: 182)
53	KV1F\$HUMAN	:QTSVRPGKVRSEPOKK*	(SEQ ID NO: 183)
54	KV1G\$HUMAN	:QTSVRPGKVRSEPEKK*	(SEQ ID NO: 184)
55	KV1K\$HUMAN	:QTSVRPGKVRSEBPZKK*	(SEQ ID NO: 185)
56	KV1D\$HUMAN	:QTSVRPGKVRSDPBKK*	(SEQ ID NO: 186)
57	KV1H\$HUMAN	:QTSVRPGQVRSDPERK*	(SEQ ID NO: 187)
58	KV1B\$HUMAN	:QTSVRPGKVRSHPEKK*	(SEQ ID NO: 188)
59	B27585	:QTSVRPGNVRSDPOKK*	(SEQ ID NO: 189)
60	NS1REIA	:QTSVRPGKVRSDPEKT*	(SEQ ID NO: 190)
61	KV1X\$HUMAN	:QTSVRPGTVRSEPEKK*	(SEQ ID NO: 191)
62	KV1L\$HUMAN	:QTSVRPEKVRSEPOKK*	(SEQ ID NO: 192)
63	IMGL38	:QTSVRPGKVRSESDKK*	(SEQ ID NO: 193)
64	A27585	:QTSVRPGVVRSEPOKK*	(SEQ ID NO: 194)
65	KV1N\$HUMAN	:QTSVRPGBVRSEBPZKK*	(SEQ ID NO: 195)
66	KV1C\$HUMAN	:QTSVSPGKVRSDPEKK*	(SEQ ID NO: 196)
67	KV1V\$HUMAN	:QTSVRPGKVRSDPEKK*	(SEQ ID NO: 197)
68	KV1T\$HUMAN	:QTSVRPGKVRSDPOTK*	(SEQ ID NO: 198)
69	KV1U\$HUMAN	:QTSVRPKKVRSDPZKK*	(SEQ ID NO: 199)
70	KV1A\$HUMAN	:QTSVRPKKVRSDPEKK*	(SEQ ID NO: 200)
71	KV1S\$HUMAN	:QTSVRSGKVRSEPETK*	(SEQ ID NO: 201)
72	KV4A\$HUMAN	:VTNLRPGKVRSDAEKK*	(SEQ ID NO: 202)
73	KV4C\$HUMAN	:VTDLRPGKVRSDAEKK*	(SEQ ID NO: 203)
74	HUMIGK2A1	:QTSVSPGNIRSESDKK*	(SEQ ID NO: 204)
75	HUMIGKBA	:KTSVTPGKVRSEPEKK*	(SEQ ID NO: 205)
76	HUMIGKBC	:VTLLPPGRVRSDAEKK*	(SEQ ID NO: 206)
77	KV2B\$HUMAN	:VTLLPPGEVRSDAEKK*	(SEQ ID NO: 207)
78	KV2D\$HUMAN	:VTLLPPGZVRSDAEKK*	(SEQ ID NO: 208)
79	KV2C\$HUMAN	:VTLLPPGZVRSDAEKK*	(SEQ ID NO: 209)
80	KV2E\$HUMAN	:VTLLPPGQVRSDAEKK*	(SEQ ID NO: 210)
81	S03876	:VTLLPPGQVTSDAEKK*	(SEQ ID NO: 211)
82	KV2A\$HUMAN	:VTLLPPAGQVRSDAEKK*	(SEQ ID NO: 212)
83	HUMIGLANS	:ALSPSSGQSSSASERL*	(SEQ ID NO: 213)

MOUSE HEAVY CHAIN SURFACE PATCHES

	1	MUSIGHIT	:EKVGGLOPGRGTPGKASRGDSQRPES*	(SEQ ID NO: 214)
5	2	MUSIGHIU	:EKVGGLOPGRGTPGKVSRGDSQRPES*	(SEQ ID NO: 215)
	3	MUSIGHIV	:EKVGGLOPGTGAPGKASRGDSQRPES*	(SEQ ID NO: 216)
	4	MUSIGHYM	:EKVGGLOPGRGTPGKASKGNSQRAES*	(SEQ ID NO: 217)
	5	PU0003	:EKVGGLOPGRGTPGKASKGNSQRAES*	(SEQ ID NO: 218)
	6	MUSIGHFO	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 219)
	7	AJ0515	:EKVGGLOPGRGTPGKASKGTSQRAET*	(SEQ ID NO: 220)
10	8	PL0018	:EKVGGLOPGRGTPGKASKGTSQRAET*	(SEQ ID NO: 221)
	9	MUSIGHFK	:ENVGGLOPGRGTPGKASKGTSQRAET*	(SEQ ID NO: 222)
	10	MUSIGHFQ	:EKVGGLOPGRGTPGKASKGTSQRAET*	(SEQ ID NO: 223)
	11	PU0001	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 224)
	12	EJ0540	:EKVGGLOPGRGTPGKASKGTSQRAER*	(SEQ ID NO: 225)
	13	HV17\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 226)
15	14	MUSIGHLN	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 227)
	15	MUSIGHKG	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 228)
	16	PU0004	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 229)
	17	MUSIGHKJ	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 230)
	18	HV56\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 231)
	19	C27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 232)
20	20	MUSIGHAAP	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 233)
	21	PH0097	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 234)
	22	E27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 235)
	23	MUSIGHJB	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 236)
	24	MUSIGHADL	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 237)
	25	A27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 238)
25	26	H27887	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 239)
	27	B27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 240)
	28	B27889	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 241)
	29	D27889	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 242)
	30	HV55\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 243)
	31	MUSIGHAGT	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 244)
30	32	MUSIGHV50	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 245)
	33	MUSIGHIW	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 246)
	34	MUSIGHAGZ	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 247)
	35	PH0098	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 248)
	36	MUSIGHID	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 249)
	37	MUSIGHAGY	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 250)
35	38	MUSIGHMF	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 251)
	39	D27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 252)
	40	MUSIGHIP	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 253)
	41	MUSIGHAGS	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 254)
	42	HV16\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 255)
	43	B34871	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 256)
40	44	PH0094	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 257)
	45	PH0096	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 258)
	46	MUSIGHV62	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 259)
	47	MUSIGHAGR	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 260)
	48	HV58\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 261)
	49	H27888	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 262)
45	50	HV34\$MOUSE	:EKVGGLOPGRGTPGKASKGTSQRAES*	(SEQ ID NO: 263)

51	HV33SMOUSE	:EKEGGLQPGKGTPEKESKGDSEKRPET*	(SEQ ID NO: 264)
52	MUSIGH2AB	:EKEGGLQPGKGSPEKESKGDSEKRAET*	(SEQ ID NO: 265)
53	N54FABH	:EKDGGGLQPGKGTPEKDSKGDSEKRVEM*	(SEQ ID NO: 266)
54	I27888	:EQVGGLKPGRGTPKEDTTGDAQRSET*	(SEQ ID NO: 267)
55	G27888	:EQVGGLKPGRGTPKEDTTGNAGKSET*	(SEQ ID NO: 268)
56	HV59SMOUSE	:EKVGGGSKPGKGTPEKDSKGNAKTSET*	(SEQ ID NO: 269)
57	MUSIGHOE	:SDQGGGLKPGKGTPEKDTKGNARRSES*	(SEQ ID NO: 270)
58	N52FVWH	:EKIGGLQPGKGDPCPKPSKDNAKRSET*	(SEQ ID NO: 271)
59	MUSIGHJT	:EKLGGGLQPGKGDPCPKPSKDNAKRSET*	(SEQ ID NO: 272)
60	MUSIGHLY	:EKLGGGLQPGKGDPCPKPFKDNAKRSET*	(SEQ ID NO: 273)
61	S06816	:EKLGGGLQPGKGDPCPKLXENAKRSET*	(SEQ ID NO: 274)
62	S06817	:ENLGGGLQPGKGDPCPKLXENAKRPET*	(SEQ ID NO: 275)
63	MUSIGHAAI	:EKLGGGLQPGNGDLGKPSKDNAKRSET*	(SEQ ID NO: 276)
64	HV42SMOUSE	:EKLGLPLQLGKGDPCPKSKDDAKRSET*	(SEQ ID NO: 277)
65	MUSIGHAAL	:EQLGGGLQPGGGTPGKPSKDNDRKSET*	(SEQ ID NO: 278)
66	MUSIGHABO	:EQLGGGLQPGGGTPGKASKDNDRKSET*	(SEQ ID NO: 279)
67	MUSIGHGEG	:EQVGGLKARKGTPEKDTTGNAGKSET*	(SEQ ID NO: 280)
68	MUSIGHWN	:EMVGVLPGKGTPEKQEGNAKRSET*	(SEQ ID NO: 281)
69	MUSIGKCLT	:EQVGGLQPKKGSFGKDSKDDSQKTET*	(SEQ ID NO: 282)
70	MUSIGHZAE	:EQVGGLQPKKGSFGKDSKDDSQKTER*	(SEQ ID NO: 283)
71	MUSIGHAAD	:QQVPELKPGRGTPGKEDKGTSAKNDT*	(SEQ ID NO: 284)
72	MUSIGHAAM	:QQVPELKPGRGTPGKDDKGTSAKNET*	(SEQ ID NO: 285)
73	MUSIGHAMA	:QQVPELKPGRGTPGKDDKGTSAKNEH*	(SEQ ID NO: 286)
74	MUSIGHXZ	:QQQPELKPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 287)
75	A30502	:EQQPELKPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 288)
76	MUSIGHAAG	:EQQPELKPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 289)
77	B30502	:EQQPELKPGRGTPGQEKKGKSSASES*	(SEQ ID NO: 290)
78	MUSIGHADG	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 291)
79	MUSIGHFV	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 292)
80	MUSIGHAANA	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 293)
81	MUSIGHZR	:EQQPELKPGRGTPGKQKKGKSSASES*	(SEQ ID NO: 294)
82	MUSIGHAI	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 295)
83	MUSIGHALA	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 296)
84	PL0011	:EQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 297)
85	MUSIGKCLS	:EQQAEELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 298)
86	MUSIGHADY	:EQQAEELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 299)
87	MUSIGHWVX	:QQQAEELRPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 300)
88	MUSIGHADO	:QQQAEELRPGRGTPGQEKKGKSTSDS*	(SEQ ID NO: 301)
89	MUSIGHVEN	:QQQAEELRPGRGTPGQEKKGKSTSDS*	(SEQ ID NO: 302)
90	A24672	:QQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 303)
91	MUSIGHJG	:QQQPELKPGRGTPGKQKKGKSTSES*	(SEQ ID NO: 304)
92	JL0044	:EQQPEAKPGKGTGKQKKGKSTSDS*	(SEQ ID NO: 305)
93	MUSIGHBA	:QQQAEELKPGRGTPGKQKKGKSTSDS*	(SEQ ID NO: 306)
94	MUSIGHAGP	:QQQAEELRPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 307)
95	MUSIGHVBK	:QQQAEELKPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 308)
96	A36194	:EQQAEELRAGKGTGQEKKGKSTSES*	(SEQ ID NO: 309)
97	MUSIGHVBJ	:EQQAEELRPGRGTPGQEKKGKSTSES*	(SEQ ID NO: 310)
98	MUSIGHADV	:QQQAEELRPGRGTPGHEKKGKSTSES*	(SEQ ID NO: 311)
99	MUSIGHAAT	:QQQAEELKPGRGTPGHEKKGKSTSES*	(SEQ ID NO: 312)
100	MUSIGHJL	:QQQAEELRPGRGTPGHEKKGKSTSES*	(SEQ ID NO: 313)

101	MUSIGHABM	:QQQAEVRPGKGTGPGHEKKGTSSTSES*	(SEQ ID NO: 314)
102	MUSIGHFU	:QQQAEKPGKGTGPGHENKGTSSSTSES*	(SEQ ID NO: 315)
5	103 MUSIGHZZB	:QQQAEKPGKGTGPGQKKGKSSASES*	(SEQ ID NO: 316)
104	HV06\$MOUSE	:HQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 317)
105	MUSIGHRD	:EQQVELRAGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 318)
106	MUSIGHVBH	:EQQAEKPGKGTGPGQEKQGTSSSTSES*	(SEQ ID NO: 319)
107	HV01\$MOUSE	:EQQAEKPGKGTGPGHDNKGTSSTSES*	(SEQ ID NO: 320)
108	MUSIGHADN	:QQQAEVRPGKGTGPGHEKKGTSSTSES*	(SEQ ID NO: 321)
10	109 HV05\$MOUSE	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 322)
110	MUSIGHAEP	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 323)
111	MUSIGHAAN	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 324)
112	MUSIGHAAB	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 325)
113	C30560	:QHQAELKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 326)
114	PS0024	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 327)
15	115 MUSIGHRG	:EQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 328)
116	MUSIGHAAB	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 329)
117	MUSIGHLX	:QQQSELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 330)
118	HV04\$MOUSE	:QQQTELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 331)
119	MUSIGHVBG	:EQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 332)
20	120 MUSIGHDX	:QQQAEKPGKGTGPGQKKGKSSSTSES*	(SEQ ID NO: 333)
121	MUSIGHAAR	:EQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 334)
122	HV15\$MOUSE	:QQQPEVRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 335)
123	MUSIGHAAU	:QQQPEVRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 336)
124	MUSIGHVBO	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 337)
125	A26405	:EQQTELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 338)
25	126 HV10\$MOUSE	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 339)
127	MUSIG3B44	:QQQSELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 340)
128	MUSIG3B62	:QQRAELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 341)
129	HV09\$MOUSE	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 342)
130	MUSIGKLP	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 343)
131	MUSIGBH	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 344)
30	132 HV11\$MOUSE	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 345)
133	MUSIGHMC	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 346)
134	MUSIGHAGW	:QQQPEVRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 347)
135	MUSIGHAP	:EQQAEVRAGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 348)
136	MUSIGHVAD	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 349)
137	MUSIGHVAF	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 350)
35	138 PL0012	:QQQPEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 351)
139	MUSIGGVD2	:QQQTELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 352)
140	S06824	:QHQAELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 353)
141	MUSIGHRS	:EQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 354)
142	MUSIGHAAB	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 355)
143	MUSIGHRS	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 356)
40	144 MUSIGHAXA	:EQQTVLRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 357)
145	HV50\$MOUSE	:QQQTELKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 358)
146	MUSIGHVBP	:QQQSVLRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 359)
147	PH0100	:LQQPVLRPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 360)
148	MUSIGHAYA	:EQQPEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 361)
149	MUSIGHCP2	:QQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 362)
45	150 MUSIGHD2	:EQQAEKPGKGTGPGQEKKGKSSSTSES*	(SEQ ID NO: 363)

151	MUSIGHNPI	:EQQAELRPGKGNPEQPKQGTSTTSET*	(SEQ ID NO: 364)
152	S06823	:EQQAELKPGKGNPEQPKQGTSTTSET*	(SEQ ID NO: 365)
153	MUSIGHASA	:EQQAELKPGKGNPEQPKQGTSTTSET*	(SEQ ID NO: 366)
154	S01484	:EQQAELKPGKGNPEQPKQGTSTTSGT*	(SEQ ID NO: 367)
155	MUSIGHVAA	:EQQAELVPGKGNPEQPKQGTSTTSET*	(SEQ ID NO: 368)
156	MUSIGHNPD	:EQQAELRPGKGNPEQPKQVTSTTSET*	(SEQ ID NO: 369)
157	MUSIGHNPS	:EQQAELRPGKGNPEQPKQITSTTSET*	(SEQ ID NO: 370)
158	MUSIGHNHC	:EQQAELRPGKGNPEQPKQVTSTTSET*	(SEQ ID NO: 371)
159	MUSIGHNPN	:EQQAELRPGKGNPEQPKQVTSTTSET*	(SEQ ID NO: 372)
160	MUSIGHNPP	:EQQAELRPGKGNPEQPKQVTSTTSET*	(SEQ ID NO: 373)
161	MUSIGHNPE	:EQQAELKPGKGNPEQPKLITSTTSET*	(SEQ ID NO: 374)
162	A27635	:TQQAELRPGKGAPEQKKGKSTSDR*	(SEQ ID NO: 375)
163	MUSIGHXW	:QYQAELRPGKGTTPQKKGKSTSES*	(SEQ ID NO: 376)
164	MUSIGHIZA	:QQQAVLRHGKGTGKKGKSTSES*	(SEQ ID NO: 377)
165	MUSIGHEN	:QQQTLGPGKGTTPGQKKGKSTSGS*	(SEQ ID NO: 378)
166	MUSIGHRH	:EQQAELRAGKGTTPGQKKGKSTSVYFA*	(SEQ ID NO: 379)
167	HV00\$MOUSE	:EQQAELKAGKGTTPGQKKGKSTSTRSET*	(SEQ ID NO: 380)
168	N\$1P19H	:QQAELAA\$KGTTPGQKKGKSTSES*	(SEQ ID NO: 381)
169	MUSIGHZAO	:QQQTLRPGKGTTPGQKKGKSTSNLRL*	(SEQ ID NO: 382)
170	B30515	:EKVGGGQSS\$PDPGKAGKSTSORAET*	(SEQ ID NO: 383)
171	MUSIGHB	:EQQAELRPGKGNPEQPKLATPSTTSET*	(SEQ ID NO: 384)
172	E27889	:EQVGGGKPGKGTTPDKSDVKONAKSET*	(SEQ ID NO: 385)
173	MUSIGHAAC	:DQQPDLPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 386)
174	HV61\$MOUSE	:DQQPDLPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 387)
175	MUSIGHVR2	:DQQPDLPSSGSPGNPSKSTSKTAET*	(SEQ ID NO: 388)
176	PL0100	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 389)
177	MUSIGHAAO	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 390)
178	MUSIGHGA6	:DQQPGLKPSGSPGDPSTKSTSKTTET*	(SEQ ID NO: 391)
179	MUSIGHJY	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 392)
180	MUSIGHGA1	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 393)
181	MUSIGHDX	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 394)
182	HV62\$MOUSE	:DQQPGLKPSGSPGNPSKSTSKTAET*	(SEQ ID NO: 395)
183	MUSIGHAAGA	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 396)
184	MUSIGHGA5	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 397)
185	MUSIGHGA4	:DQQPGLKPSGSPGDPSTKSTSKTTET*	(SEQ ID NO: 398)
186	MUSIGHAGI	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 399)
187	PL0102	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 400)
188	HV46\$MOUSE	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 401)
189	MUSIGHET	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 402)
190	MUSIGHAGD	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 403)
191	MUSIGHAGQ	:DQQPSLKPSSGSPGNPSKSTSKTAET*	(SEQ ID NO: 404)
192	MUSIGHAM32	:DQQPDLPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 405)
193	MUSIGHAFK	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 406)
194	MUSIGHAGE	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 407)
195	MUSIGHAGB	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 408)
196	MUSIGHAGC	:DQQPSLKPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 409)
197	MUSIGHAAM	:DQQPGLKPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 410)
198	HV43\$MOUSE	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 411)
199	MUSIGHMUV1	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 412)
200	MUSIGHAEI	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 413)
201	MUSIGHBP	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 414)
202	MUSIGHZ2A	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 415)
203	MUSIGHUV2	:DQQPGLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 416)
204	A32456	:DQQPVLAPSSGSPGNPSKSTSKTTET*	(SEQ ID NO: 417)
205	MUSIGHMB	:DQQPSLQPSGSPGNPSKSTSKTTET*	(SEQ ID NO: 418)

HUMAN HEAVY CHAIN SURFACE PATCHES

1	HUMIGHVS	: ERVGDLEPCRGIPGKAPKGDSSKKTET*	(SEQ ID NO: 419)
2	HUMIGHVR	: ERVGDLEPERGIPGKAPKGDSSKKTET*	(SEQ ID NO: 420)
5	3 H36005	: EQVGGLQPGRGTPGKAPKGDSSKKTET*	(SEQ ID NO: 421)
4	PL0122	: EQVGGLQPGKGTSGKASKGDSSKKTET*	(SEQ ID NO: 422)
5	HV1DSHUMAN	: EQLGGLQPGRGTPGKBSKGDSSKRAET*	(SEQ ID NO: 423)
6	HUMIGHAT	: EQLGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 424)
7	B34964	: EQLGGLQPGRGTPGKDSRGNSKRAET*	(SEQ ID NO: 425)
8	A34964	: EQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 426)
10	9 PL0123	: EQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 427)
10	HV1FSHUMAN	: EQVGGLQPGRGTPGKDSKGDSSRAET*	(SEQ ID NO: 428)
11	JL0048	: EQVGGLQPGRGTPGKDSKGNSSRAET*	(SEQ ID NO: 429)
12	HV1BSHUMAN	: QQVGGLQPGRGTPGKDSKGBSSKRAET*	(SEQ ID NO: 430)
13	HUMIGHBV	: EQLGDLQPGRGTPGKASKGNSSKRAET*	(SEQ ID NO: 431)
14	HV1ESHUMAN	: EQVGGLQPGRGTPGKDSKGDSSKRAET*	(SEQ ID NO: 432)
15	15 PL0116	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 433)
16	HV1KSHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRPET*	(SEQ ID NO: 434)
17	N92FB4H	: EQVGGLQPGRGTPGKDSKGDSSKRPET*	(SEQ ID NO: 435)
18	HV1ISHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRPET*	(SEQ ID NO: 436)
19	HV1JSHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRTET*	(SEQ ID NO: 437)
20	HV1GSHUMAN	: QQVGGLQPGRGTPGKDSKGBSSKRAET*	(SEQ ID NO: 438)
21	HV1MSHUMAN	: EQLGGLQPGRGTPGKDSKGNSSKQAZT*	(SEQ ID NO: 439)
22	HV1OSHUMAN	: EQLGGLQPGRGTPGKDSKGNSSKQAZT*	(SEQ ID NO: 440)
23	HV1NSHUMAN	: AQLGGLQPGRGTPGKDSKGNSSKQAZS*	(SEQ ID NO: 441)
24	HV1RSHUMAN	: EQLGGLQPGRGTPGKDSKGNSSKQAZT*	(SEQ ID NO: 442)
25	HV1PSHUMAN	: EQVGGLQPGRGTPGKDSKGNSSKQAZT*	(SEQ ID NO: 443)
26	HUMIGHCV	: EQLGGLQPERGTPGKESKGNSSKRAET*	(SEQ ID NO: 444)
27	HV1TSHUMAN	: EQVGDLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 445)
28	HV1USHUMAN	: EQVGDLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 446)
29	PL0098	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 447)
30	HV1HSHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 448)
31	HV1ASHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 449)
32	HV1SSHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 450)
33	HUMIGHAW	: EQLGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 451)
34	HV1QSHUMAN	: EQVGALQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 452)
35	A36040	: EQLGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 453)
36	HUMIGHAM	: EQVGALQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 454)
37	HUMIGHAB	: EQVGALQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 455)
38	HUMIGHAL	: EQVGALQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 456)
39	HV1LASHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 457)
40	HV1ASHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 458)
41	A32483	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 459)
42	HUMIGHAY	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 460)
43	HUMIGHCU	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 461)
44	HUMIGHBS	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 462)
45	HUMIGHLS	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 463)
46	HUMIGHBX	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 464)
47	HV1CASHUMAN	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 465)
48	H34964	: QQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 466)
49	HUMIGHCY	: EQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 467)
50	PL0119	: EQVGGLQPGRGTPGKDSKGNSSKRAET*	(SEQ ID NO: 468)

51	HV1F\$HUMAN	:QQVAEVKPCRGRDPGRPRQASSTISAT*	(SEQ ID NO: 469)
52	D34964	:EQVAEVPQCKGRPGKSLQCKSLKAST*	(SEQ ID NO: 470)
53	HV1D\$HUMAN	:QQMAEVKPCRGTGKPGVVPSPFFSET*	(SEQ ID NO: 471)
54	HV1E\$HUMAN	:QQVAEVKPCRGTGPGRYIWEPSFFNEG*	(SEQ ID NO: 472)
55	JL0047	:QQQAGLKPSGSGPGKPSKSTSKTAAT*	(SEQ ID NO: 473)
56	HUMIGHBW	:QQQPGLKPSGSGPGKPSKSTSKTAAT*	(SEQ ID NO: 474)
57	E34964	:QQQPGLKPSGSGPGKPSKSTSKTAAT*	(SEQ ID NO: 475)
58	HUMIGHCW	:QQQPGLKPSGSGSAGKPSKSTSKTAAT*	(SEQ ID NO: 476)
59	HV2F\$HUMAN	:RQQPGLKPSGSGPGKPSRGTSSRSAAT*	(SEQ ID NO: 477)
60	HV2I\$HUMAN	:QQQAGLKPSGSGPGRTSKSTSKTAAT*	(SEQ ID NO: 478)
61	HV2G\$HUMAN	:QQEPGLRPSGSGTSGRTSKSTSKTAAT*	(SEQ ID NO: 479)
62	NS3FABH	:XQEPGLRPSGSGPGRTSKSTSKTAAT*	(SEQ ID NO: 480)
63	PS0091	:QQQPGLKPSGSGSPSRVSKSTSKTFET*	(SEQ ID NO: 481)
64	HUMIGHDA	:QHQAAGLRSSGSGPGKPSSTSTSKTAAT*	(SEQ ID NO: 482)
65	A26555	:ZQESGLKPTSGSGPGKPSKSRSKAADA*	(SEQ ID NO: 483)
66	HV2E\$HUMAN	:QTKPTLKPTTGSPGRPSKSTSKDPVT*	(SEQ ID NO: 484)
67	HV2D\$HUMAN	:QTKPTLKPTTGSPGKPSRSTSRDPVS*	(SEQ ID NO: 485)
68	A36005	:ETRPALKPTTGSPGKTSKTTSKDPVT*	(SEQ ID NO: 486)
69	HV2H\$HUMAN	:QNRPALKATTGSPGKTSKTTSKDPAT*	(SEQ ID NO: 487)
70	HV2A\$HUMAN	:QTPPALKPTTGSPGKTSKTTSDSKNPVT*	(SEQ ID NO: 488)
71	HV2C\$HUMAN	:QTRPALRPTTGSPGKTSKTTSKGPGCT*	(SEQ ID NO: 489)
72	HV2B\$HUMAN	:QTRPALKPTTGSPGKTSKTTSDRTAY*	(SEQ ID NO: 490)
73	JL0049	:LEGVQLWGGRGISRKYARGNGKRDSE*	(SEQ ID NO: 491)

EXAMPLE 2

DETAILED DESCRIPTION OF METHOD FOR CONSTRUCTING THREE-DIMENSIONAL MODEL OF ANTIBODY VARIABLE REGION

[0070] The references cited in the text below are listed at the end of this Example.

[0071] The first antibody Fab structure was determined in 1972. Since then, no more than about twelve Fab structures have been published, a number that represents a very small fraction of the total antibody repertoire ($>10^8$ antibodies). To understand the molecular basis of this antibody diversity will require knowledge of either a large number of x-ray structures, or the rules by which combining site topography is governed. The development of such prediction rules has now reached the point where variable regions of antibodies can be modelled to an accuracy approaching that of the medium resolution x-ray structure.

[0072] The interaction of an antibody with its cognate antigen is one of the most widely accepted paradigms of molecular recognition. To understand the antibody-antigen interaction in atomic detail requires knowledge of the three-dimensional structure of antibodies and of their antigen complexes. Traditionally such information has come from x-ray crystallographic studies (see Davies et al. for review (Davies et al., 1988)).

[0073] The modelling of antibody combining sites was first attempted by Padlan & Davies (Padlan et al., 1976) at a time when very few antibody structures were known. Nonetheless, Padlan and colleagues recognized that the key lay in high structural homology that existed within the β -sheet framework regions of different antibody variable domains. The antigen combining site is formed by the juxtaposition of six interstrand loops, or CDRs (Complementarity Determining Regions) (Kabat et al., 1987), on this framework. If the framework could be modelled by homology then it might be possible to model the CDRs in the same way. Padlan and Davies (Padlan et al., 1976) reasoned that CDR length was the important determinant of backbone conformation though the number of antibody structures was insufficient to thoroughly test this maximum overlap procedure (MOP). This notion was not picked up again until the early 1980's when Pedersen and Rees proposed a similar approach to modelling antibody combining sites based on a more extensive analysis of antibody structures (de la Pas et al., 1986).

[0074] Those essentially knowledge-based procedures are best exemplified for antibodies by the work of Chothia & Lesk (Chothia et al., 1986) who, in 1986, extended and modified the MOP procedure by introducing the concept of "key" residues. These residues allow the further subdivision of CDRs of the same length into "canonical" structures which differ in having residues at specified positions that, through packing, hydrogen bonding or the ability to assume unusual values of the torsion angles ϕ , ψ and ω , determine the precise CDR conformation (Chothia et al., 1989). Similar knowledge-based methods have been proposed for predicting loop conformations in general (Thornton et al., 1988; Tramontano et al., 1989). These methods rely on the crystallographic database of protein structures. However, none of the above knowledge-based methods has been totally successful. In particular, the MOP or canonical structure approaches have succeeded in modelling only five of the six CDRs. This stems from the fact that the third CDR of the

heavy chain, H3, is more variable in sequence, length and structure than any of the other CDRs.

[0075] To deal with this problem several groups have attempted to use *ab initio* methods to model the combining site (Brucoleri and Karplus, 1987). The requirement with such methods is that the total allowable conformational space accessible to a particular CDR is sampled. Typical of purely geometric approaches is that of Go & Sheraga (Go and Sheraga, 1970) and more recently Palmer & Sheraga (Palmer and Sheraga, 1991), where the problem is reduced to one in which the central region of the polypeptide backbone, having characteristic bond length and bond angles, is constructed between the end points of the loop (CDR if an antibody loop) by a "chain closure" algorithm. In a modification of this algorithm, Brucoleri & Karplus (Brucoleri and Karplus, 1987) introduced an energy minimization procedure which greatly expanded the domain of conformational space searched during the chain closure procedure. This modification is incorporated into the conformational search program CONGEN (Brucoleri and Karplus, 1987), which also allows the user to choose any set of standard bond length and bond angles such as the CHARMM (Brooks et al., 1983) standard geometry parameter sets. Other approaches such as minimization (Moult and James, 1986), or molecular dynamics (Fine et al., 1986) either fail to saturate conformational space or are unable to deal with the problem of long CDRs. Whichever of the *ab initio* methods is employed however, the problem is one of defining the selection criteria in such a way as to allow the unambiguous identification of the correct structure (in this context correct is defined by reference to an appropriate X-ray structure) within the ensemble of candidates, for every CDR. To date this has not been possible.

[0076] Recently a more holistic approach has been taken to the modelling of CDRs which combines the advantages of knowledge-based and *ab initio* methods in a single algorithm known as CAMAL (Combined Algorithm for Modelling Antibody Loops) (Martin et al., 1989; Martin et al., 1991). Previously this algorithm has been used to model individual CDRs in the presence of the crystal structure conformations of the other five. As is demonstrated below, CAMAL is able to predict the backbone conformations of all six CDRs of the antibody combining site to an accuracy approaching that of medium resolution x-ray structures. In addition the algorithm includes a procedure for selecting and fitting together the light and heavy chain framework regions prior to generation of CDR conformations, thus making possible the prediction of the entire variable region. Furthermore a new Monte Carlo (MC) simulated annealing method has been developed for the determination of sidechain conformations.

The Framework Region

[0077] Antibody framework regions consist of conserved β -strands that form the β -barrel structure characteristic of immunoglobulin V-type regions. In the procedure described here each V-region is built from a database of known antibody structures, using sequence homology for selection of the light (L) and heavy (H) chain V-domains. The two domains are then paired by least squares fitting on the most conserved strands of the antibody β -barrel (Table 2 and Figures 5 & 6). The strand orientations were determined by analyzing the barrels of known antibody crystal structures. Eight antibodies were analyzed using a multiple structure fitting program as follows. Seven structures were fitted onto one of the set selected at random and mean coordinates were calculated. All eight structures were then fitted onto these mean coordinates and new mean coordinates determined. This procedure was iterated until the mean coordinate set converged (5-10 cycles). The variance for the mean coordinates at each barrel point (N,C α ,C) was calculated. In Figure 5 this variance is plotted against the projected positions of these points onto the conjugate axis of the barrel.

[0078] Strand 8 and all but two residues of strand 7 in both light and heavy chains were eliminated as they showed deviations greater than 3σ (standard deviation units) from the mean coordinates. These two strands comprised the takeoff points of CDR H3, and suggests that any knowledge-based prediction of CDR H3 would have to account not only for sequence and length variation in the CDR itself, but also for the position of the participating strands. The remaining mean coordinates were used as a scaffold onto which the L and H chains were fitted. Strands 7 and 8 in the final framework were obtained from the database structure used in the construction. The framework strands are marked + in the multialignment in Table 2.

[0079] The sidechains were then replaced using a 'maximum overlap' method, in which sidechain templates were fitted on backbone atoms with the sidechain torsion angles being adjusted to match those of equivalent torsions in the parent sidechain.

The Combining Site

[0080] The procedure for predicting the structure of combining sites combines a database search with a conformational search procedure. The architecture of the program suite to perform this task is outlined in Figure 7.

[0081] The database search utilizes distance constraints for each of the six CDR loops determined from known antibody structures. These constraints were determined by calculating C α -C α distances within known loops and using a search range of $\bar{x} + 3.5\sigma$ (the mean \pm 3.5 standard deviation units). A database containing all the proteins in the Brookhaven Protein Databank (Bernstein et al., 1977) is then searched for fragments which satisfy the constraints for

a loop of the required length. The middle section of the loop is then deleted and reconstructed using the conformational search program CONGEN (Brucoleri and Karplus, 1987). For loops of six or seven residues, the structure database appears to saturate the conformational space available to the backbone adequately and only sidechains are built by conformational search. Loops shorter than six residues are built by conformational search alone since this is computationally feasible and the number of loops selected from the database becomes unacceptably large as loop length decreases.

[0082] When modelling a complete combining site, loops of 6 or more residues are modelled individually with the other loops absent. If the loops are built consecutively, small errors can accumulate leading to a poor result (Martin, 1990). All the loop conformations are then evaluated using a solvent modified potential, which excludes the attractive van der Waals and electrostatic terms of the non-bonded energy function contained within the GROMOS (Åqvist et al., 1985) potential. The lowest five energy conformations are selected and filtered using a "structurally determining residue" algorithm (FILTER), based on backbone torsion angles observed in the original database loops. Since the database search is not used for the shortest loops of 5 residues or fewer, the FILTER algorithm cannot be used. Energy is thus the only available selection criterion and the short loops are built last, in the presence of the longer loops.

Side Chains

[0083] The determination of sidechain positions was previously done using the iterative sidechain determination algorithm described by Brucoleri et al. (Brucoleri and Karplus, 1987). Unfortunately the CHARMM (Brooks et al., 1983) force field fails to select the correct conformations of exposed hydrophobic sidechains. There is no penalty for having an exposed uncharged atom, without solvent present. CONGEN is also unable to saturate the conformational space for a large number of sidechains (more than 6 residues).

[0084] Recently Lee et al. (Lee and Levitt, 1991; Lee and Subbiah, 1991) has proposed a method for searching conformational space for a large number of sidechains using MC simulated annealing. A simple energy function is used for the evaluation of conformations generated by a biased random walk:

$$E = \sum_{i=1}^n \epsilon_o \left(\left(\frac{r_o}{r} \right)^{12} - 2 \left(\frac{r_o}{r} \right)^6 \right) + \kappa_o \cdot \cos(3\omega)$$

Where the first term is a simple *Lennard-Jones* potential which evaluates the non-bonded contacts between the atoms in a given molecule, the second term is a simple torsional term which only applies to C-C bonds. The torsional term biases the function towards 60° rotamers. ϵ_o and κ_o are constants. The metropolis function:

$$P = C \frac{-\delta E}{T}$$

is used to evaluate the energy function. Any move which results in a decrease in energy is accepted, and any move which results in a positive δE is only accepted with the probability P . This simple method can be used to search the large conformational space defined by a set of torsion angles in amino-acid sidechains, and find or define the global minimum which exist for a set of sidechains. T is the simulation temperature.

[0085] When searching sidechain conformations using this method the simulation system usually gets trapped in an energetic minima well before the global minimum is encountered, at a high temperature, without the solution space having been searched sufficiently. This problem can be solved by truncating the *Lennard-Jones* potential, thus allowing atoms to pass through each other. In reality this function would converge towards infinity when the distance r between the atoms approaches zero.

[0086] The evaluation of sidechain conformations generated is done solely on the basis of energy, for internal (core) residues, since good van der Waal's interactions are considered to be equal to a good packing of the sidechains. The situation becomes more complicated when trying to predict the conformation of surface residues. The lowest van der Waal's interaction is obtained by a combination of sidechain conformations which minimize the overlap of atoms, this means that the lowest energy is obtained with extended conformations of sidechains, without considering good packing of sidechains.

[0087] Using the fact that hydrophobic, bulky residues will be shielded by the hydrophilic sidechains, and will be buried in the surface, it is possible to generate a simple function which will evaluate these macroscopic observations. These functions can either be implemented in the objective evaluation function of the Monte Carlo simulation, or as is

done here, added as a post processing step. Including an accessibility/hydrophobicity term in the evaluation function would slow down the calculation considerably, hence the term has been added as a post processing function. The function used is a sum of the product of relative exposed surface area multiplied by the residual hydrophobicities. The hydrophobicities used are taken from Comette et al. (Comette et al., 1987).

$$F_{conformation} = \sum_{i=1}^n -A_{irel} \cdot H_{irel}$$

n is the number of sidechains reconstructed. The surface area is calculated using the tessellated icosahedron approach (Chau and Dean, 1987), which is not very precise (0.1 percent), but is able to evaluate a large number of conformations. The function is evaluated for the final 2,000 conformations and the lowest value conformation selected as the best.

[0088] Using this simple approach it is possible to integrate over a large phase space with many degrees of freedom, and get a complete sampling of the space.

Predicted Structures of an Anti-hapten, Anti-peptide and Two Anti-protein Antibodies

[0089] In the following section the predicted structures of four different antibody F_v regions are presented and analyzed. The antibodies are:

- Gloop-2 (Darsley and Rees, 1985), an anti-lysozyme antibody whose Fab structure was determined by Jeffrey et al., (Jeffrey et al., 1991) and which was used as a learning exercise during the development of CAMAL.
- D1.3 (Amit et al., 1986), an anti-lysozyme antibody whose uncomplexed F_v coordinates were supplied by R. Poljak et al. after the model coordinates had been deposited.
- 36-71 (Rose et al., 1990), an anti-phenylarsonate antibody whose Fab structure was carried out by D. R. Rose, et al., and whose coordinates were obtained after the model coordinates had been deposited.
- 3D6 (Grunow et al., 1988), an anti-protein (GP41 of HIV) antibody whose Fab structure was carried out by D. Carter et al. (Carter, 1991) and whose coordinates were obtained after the model coordinates had been deposited. For this antibody, the model was generated using the canonical loop method of Chothia & Lesk (Chothia et al., 1989; Chothia et al., 1986) for CDRs L1, L2, H1 and H2, while L3 and H3, which cannot be modelled using canonical structures, were constructed using CAMAL.

[0090] All four models were subjected to both restrained and unrestrained energy minimization using the DISCOVER (TM Biosym Technology) potential with 300 cycles of steepest descents, followed by conjugate gradient minimization until convergence to within 0.042J (0.01 Kcal) occurred.

[0091] The resolution and R-factors of the x-ray structures are given in Table 3 together with the parent frameworks selected in building the models. The structures and models were compared by global fits of the loops. The β -barrel strands 1 to 6, as described above, were least squares fitted and the RMS deviation was then calculated over the loops. The backbone (N,C α ,C) RMS values for fitting model and crystal structure frameworks were between 0.4 and 0.9x10⁻¹⁰m (0.4 and 0.9 Å), illustrating the conservation of the core β -barrel. Using all eight strands RMS deviations between 0.6 and 1.2x10⁻¹⁰m (0.6 and 1.2 Å) were observed.

[0092] Global fits (Table 4) give a more realistic measure of the accuracy of the model than a local least-squares fit over the loops since they account for the overall positioning of the loops in the context of the F_v structure. Local fits, which give lower RMS deviations, are also shown in Table 4. Differences between local and global RMS deviations arise from differences in V_H/V_L domain packing and differences in loop 'take off' angles and positions.

[0093] Table 5 shows the canonical loops selected from modelling 3D6. Backbone structures of the modelled CDRs, superimposed on the x-ray structures after global fitting are shown in Figure 8. General features and points of interest for each of the six CDRs are discussed below.

Analysis of the CDR Regions

[0094] During the comparison of CDR conformations in the V-region models and the x-ray Fab structures it was observed that at certain positions in a CDR, the peptide backbone may adopt either of two conformations by undergoing

a "peptide flip" (1,4 shift). This phenomenon is also seen in type 2 β -turns (Paul et al., 1990). Dynamics simulations of β -turns show that the transformation energy between $\phi_1 = -00$, $\psi_1 = -30$, $\phi_2 = -90$, $\psi_2 = 0$ and $\phi_1 = -00$, $\psi_1 = 120$, $\phi_2 = 90$, $\psi_2 = 0$ has a maximum value of 5 kcal (Paul et al., 1990). This is low enough to allow selection of either conformation. The peptide flip is observed within several canonical classes (as described by Chothia et al. (Chothia et al., 1989)) and the hydrogen bonding pattern used to determine the conformation of a canonical class does not disallow the peptide flip. Any modelling procedure should therefore take these, or any other multiple conformations, into consideration where the transformation energies are sufficiently low to permit population of the different conformational forms. Table 6 shows an example of the "peptide-flip" phenomenon from the crystallographic database of antibody structures. It should be noted that a single crystal structure will not show multiple conformations since the crystallization will 'freeze out' one of the conformations. During the modelling procedure the two populations of conformers are easily extracted from a set of ab initio generated loops, by using a torsional clustering algorithm.

CDR-L1

[0095] In Gloop-2 and D1.3, all five low energy conformations were very similar with RMS deviations differing by less than $0.25 \times 10^{-10} \text{m}$ (0.25 Å) (backbone) and $0.35 \times 10^{-10} \text{m}$ (0.35 Å) (all atoms). The FILTER algorithm was unable to distinguish between the conformations and the lowest energy structure was selected.

[0096] Although CDR-L1 of 3D6 was originally built using the canonical loop from HyHEL-10, the midsection was rebuilt by conformational search, for the following reason. HyHEL-10 and REI CDR-L1 loops are placed in the same canonical ensemble (Chothia et al., 1989) although they contain a 1-4 shift (peptide flip) relative to one another between the fifth and eighth residues of the loop (residues 28-31) (see Table 6).

[0097] 36-71 shows the same 1-4 shift between the model and crystal structure CDRs. Both crystal structure and model were compared with other loops of the same canonical class as defined by Chothia et al. (Chothia et al., 1989). It was found that the hydrogen bonding pattern which determines the conformation was conserved.

CDR-L2

[0098] CDR-L2 of D1.3 has two adjacent threonines (49, 50) which in the x-ray structure are packed against the tyrosine at the fourth position of CDR-H3, thus minimizing the exposed hydrophobic sidechains. In the unminimized model the threonine sidechains are exposed to the solvent, but after energy minimization, this packing is observed.

CDR-L3

[0099] In Gloop-2, D1.3 and 36-71 the proline at the seventh position in the loop is correctly predicted in the *cis* conformation. It has previously been suggested that the conformation of CDR-L3 is dictated by the presence of a proline in position 8 or 9 (Chothia et al., 1989) within the loop. 3D6 does not have a proline in either position. Only 7 out of 290 CDR-L3 sequences (Kabat et al., 1987) lack a proline at both positions and in all of the published x-ray structures this proline is present. This is an example of a situation where either a new canonical class may need to be defined or where the canonical rule breaks down altogether, and an alternative method must be employed.

[0100] The 3D6 L3 loop is 7 residues in length and was built using database loops alone where conformational space is saturated by means of fragments selected from the crystallographic database (Global RMS $2.01 \times 10^{-10} \text{m}$ (2.01 Å), N,C α ,C), and by using CAMAL (Construction: Q[Q(YNS)Y]S, Global RMS: $1.97 \times 10^{-10} \text{m}$ 1.97 Å, N,C α ,C). The similarity of the structures generated by the two procedures illustrates the utility of the database search and suggests that, for shorter loops it is capable of saturating the available conformational space.

CDR-H1

[0101] Using the Kabat and Wu definition of CDR-H1 places this loop as an extension of the β -sheet. The extended nature of this stretch of peptide limits its conformational flexibility and CDR-H1 is generally modelled accurately (Martin et al., 1989; Chothia et al., 1989).

[0102] In Gloop-2 and D1.3, the Phe or Tyr sidechain at the second position in the loop is poorly placed and packs against Leu at the penultimate position in HFR1 (see Table 2). 36-71 has a well-placed Asn at this position, rather than the more common bulky hydrophobic sidechain.

CDR-H2

[0103] CDR-H2 of 36-71 is similar in sequence to F19.9 (Strong et al., 1991), (36-71: YNNPGNGYIA (SEQ ID NO: 492); F19.9: YINPGKGYLS (SEQ ID NO:493)). While the structurally determining residues specified by Chothia and

Lesk (Chothia et al., 1989) are conserved, the backbone conformations are different: F19.9 has a bulge at the -PGN-Gly, compared with 36-71, giving the loop a 'kink' in the middle. The model of 36-71 shows a 1-4 shift, though the sidechains are still well placed.

[0104] In Gloop-2, the all atom RMS deviation is poor ($3 \times 10^{-10} \text{m}$) (3.00 Å) (Jeffrey et al., 1991) when compared with the P2₁ crystal structure, owing to rotations of the Phe at position 3 in the loop and Tyr at position 10 by approximately 120° about the χ_2 torsion angle. Gloop-2 has been solved in two different crystal forms, P2₁ and P1 (Jeffrey et al., 1991; Jeffrey, 1989). When compared with the P1 structure, the sidechains are placed almost perfectly and the all atom RMS (global fit) drops to $2.23 \times 10^{-10} \text{m}$ (2.23 Å).

[0105] This concerted sidechain motion between crystal forms illustrates the effects of crystallization conditions on surface sidechain placement. Even though surface sidechains may show low temperature factors indicating low mobility in the crystal, their mobility in solution may be high. In the Gloop-2 P1 structure, the mean sidechain temperature factor for the F_v domain is 13.46 ($\sigma = 8.20$) while the sidechains of these two residues of H2 show mean temperature factors of 5.56 ($\sigma = 0.68$) for the Phe at position 3 and 7.10 ($\sigma = 1.73$) for the Tyr at position 10.

CDR-H3

[0106] CDR-H3 is the most variable of the six CDR's with all lengths up to 21 residues being represented in Kabat et al., (Kabat et al., 1987). This extreme variability results from V-D-J splicing (Schilling et al., 1980) and has always been a problem when attempting to model antibodies. Such loops may be divided into short (up to 7 residues), medium (up to 14 residues) and long (15 or more residues). Using the CAMAL procedure, short and medium CDR-H3's can be modelled as accurately as other CDR's of similar lengths. Although long CDR-H3's are more difficult and cannot, at present, be built to the same accuracy, the chain trace is still correct.

[0107] It is unlikely that the longer loops consist of 'pure' loops (i.e., all random coil or turn). In crystal structures of antibodies with medium to long CDR-H3 loops (McPC603 (Rudikoff et al., 1981): 11 amino acids (aa); KOL (Marquart et al., 1980): 17 aa; F19.9 (Lascombe et al., 1989): 15 aa) the loops consist of a disordered β -sheet extension from the β -barrel core and a 5-8 residue random coil/turn connecting these two strands.

[0108] To determine the nature of medium to long loops (>8 residues) which satisfy the CDR-H3 constraints, a complete search of the Protein Databank for loops of length 8-20 residues, was performed using the inter-C α distance constraints determined from known antibody crystal structures for CDR-H3. The resulting loops were then analyzed using the DSSP (Kabsch and Sander, 1983) program, which is able to assign secondary structure to polypeptide structures. The amount of secondary structure for each length of loop was calculated, and it was observed that for loops longer than 12 residues the amount of secondary structure within each of the classes described in DSSP was constant. The number of loops selected is also constant (approximately 150 loops) for loops longer than 12 residues. A closer inspection of each of the length ensembles shows indeed that the loops are the same between the groups.

[0109] This analysis shows that, like the long CDR-H3 crystal structures, the selected fragments consist of β -strands connected by 5-8 residue loops. For loops above 12-13 residues in length, the same loops are selected, but with extensions to the β -strands. This is called the "sliding-ladder" effect. In addition, the maximum size of a random coil or turn fragment in any of the structures contained in the Protein Databank tends not to exceed 8 residues, as determined by DSSP. This implies that the conformational space of longer loops is not saturated by the database and, although it is unlikely that long loops in antibodies will differ significantly from long loops in other structures, confidence in the prediction must be correspondingly reduced.

[0110] By how much is the usefulness of the CAMAL algorithm reduced by this observation ?

[0111] The frequency of occurrence of different CDR-H3 lengths in antibody sequences described by Kabat et al. (Kabat et al., 1987) was analyzed. Figure 10 shows that more than 85% of H3 loops have lengths between 4 and 14 residues which can be modelled accurately by the CAMAL algorithm.

[0112] CDR-H3 of D1.3 is of average length (8 residues), though no loops of this length are seen in the available antibody structures. The crystal structure coordinate set showed an RMS of $1.9 \times 10^{-10} \text{m}$ (1.9 Å) compared with the model.

[0113] The 36-71 loop is 12 residues long. The conformation is correctly predicted as a short loop connecting an extension of the β -sheet.

[0114] The 3D6 H3 loop is 17 residues long. While KOL (Marquart et al., 1980) has the same length it has only one residue in common with 3D6 and only one conservative mutation. There is thus no reason to believe that the conformations would be similar. The final predicted conformation of 3D6 is an extended β -sheet, as in the crystal structure. The difference between the predicted and the crystal structure of 3D6-H3 is due to a twist of 5-7° in the extended β -sheet loop (see Figures 9A-9D). Such a twist has also been observed for complexed and uncomplexed antibodies by Wilson et al. (Wilson and others). This suggests that long CDR-H3 loops may be flexible and actively involved in antigen binding.

The Complete Variable Region

[0115] Prediction of the strand positions and V_L - V_H orientation in the framework β -barrel was exact for all of the four antibodies. The backbone (N,C α ,C) RMS deviations from the crystal structures were between 0.56 and 0.86x10⁻¹⁰m (0.56 and 0.86 Å), despite the fact that, in all cases the V_L and V_H regions of a particular model were derived from different antibody structures. This suggests that this method will do well in procedures such as humanization (German et al., 1991), where correct framework positioning is important. The backbones of all six CDRs in all four antibodies are essentially correctly predicted, as shown in Figure 8. There are two important points to make about these predictions. First, the position of each CDR on its framework barrel is correct. Thus, CDR-framework interactions can be confidently monitored. The only deviation from the x-ray structure is CDR-H3 of antibody 3D6 which has been previously discussed. Second, the all atom RMS deviation between models and x-ray structures is dominated by sidechain positions. In most instances this deviation is due to a small number of incorrectly positioned, exposed sidechains (for example, in D1.3 the only sidechains which are incorrectly predicted are Tyr 9 of L1, Trp 4 of L3, Tyr 2 of H1 and Tyr 4 of H3). Since each CDR is constructed in the absence of other CDRs, the force field may choose a rotamer which is 120° away from that found in the crystal structure. This effect has also been observed by Lee et al. (Lee and Levitt, 1991).

Conclusion

[0116] For antibodies having CDR H3 regions of 14 residues or less the complete variable domain can be modelled to an accuracy approaching that of medium resolution x-ray structures. For antibodies with longer H3 loops the CAMAL algorithm is likely to need an additional procedure in which molecular dynamics simulations are also incorporated.

[0117] The canonical approach of Chothia et al. appears to work well (at least in modelling backbones) where it may be applied and may be used successfully in combination with the CAMAL procedure.

[0118] One important observation that has emerged from these studies is that a given loop can exist in several conformations. In particular, this seems likely for CDR-L1 and, to a lesser extent, CDR-L3 and longer CDR-H3's. A simple combinatorial calculation shows that, if each of these three loops can exist in three separate conformations, a given combining site can have $3^3 = 27$ different topographies. Clearly, this would explain the origins of cross reactivity and would allow for induced fit of antigens.

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Table 2: Alignment of antibody sequences used in the modelling. '*' indicates CDR regions; '+' indicates β -strand regions used in the fitting for modelling frameworks. Nomenclature for β -barrel strands is (H or L - Chain) - FR(Framework region)-(Strand number), thus for example strand one of the heavy chain becomes HFRL.

Table 3:

Details of the antibody crystal structures against which the models were compared and the parent frameworks used to build the models. Resolution data for D1.3 has not yet been published.

Antibody	Resolution	R-factor	Framework Model	
			Light	Heavy
Gloop-2	2.80	21.2	REI	HyHEL-5
D1.3	-	-	REI	NEW
36-71	1.90	20.9	Gloop2	NEW
3D6	2.70	17.7	REI	KOL

Antibody	CDR	sequence	SEQ ID NO	RMS local (Å)			RMS global (Å)		
				Ca	N,Ca,C	All MC	Ca	N,Ca,C	All MC
Glloop-2 D1.3 36-71 3D6	L1	RASIQ(EIS)QVLS RASIQ(NIH)YLA RASIQ(DIN)PLN RASIQ(SIQ)NMLH	494 495 496 497	0.73 2.38 2.71 0.81	0.71 1.93 2.43 0.84	3.08 4.38 4.80 3.48	1.84 3.94 4.58 1.93	0.88 3.72 3.41 0.61	0.87 3.48 3.31 0.78
Glloop-2 D1.3 36-71 3D6	L2	AASITLDS YIT(TTL)AID PITSRS)QIS KASSLES	498 499 500 501	0.38 0.87 0.66 0.41	0.33 0.73 0.68 0.42	0.80 1.80 3.84 1.37	1.00 1.40 3.38 1.30	0.68 0.78 0.78 0.63	0.68 1.02 0.72 0.66
Glloop-2 D1.3 36-71 3D6	L3	LQV(LSY)PLT QHIF(WST)PRT QIQ(NAL)PIRT QIQVNS)YIS	502 503 504 505	0.56 1.41 1.01 1.08	0.62 1.35 1.00 1.08	1.70 3.88 3.36 3.84	1.80 3.88 3.10 3.80	0.78 1.78 1.48 2.81	0.74 1.70 1.36 1.87
Glloop-2 D1.3 36-71 3D6	H1	IT(FGI)TI IQ(VGV)NI IS(NGI)NI DYAMH	506 507 508 509	0.40 0.44 0.46 0.47	0.70 0.62 0.63 0.17	3.00 3.88 3.32 1.82	1.80 2.00 1.96 1.11	1.08 0.68 1.06 0.61	1.01 0.60 0.87 0.72
Glloop-2 D1.3 36-71 3D6	H2	ELF(PON)SKTY MIW(QDO)NTD YNNP(QNQ)YIA ISWDSSIO	510 511 512 513	0.53 0.42 0.44 0.48	0.64 0.62 0.78 0.82	1.68 1.88 3.01 2.38	1.70 1.40 3.38 2.88	1.38 0.87 1.47 0.98	0.88 0.88 1.41 0.88
Glloop-2 D1.3 36-71 3D6	H3	IR(EIR)VI ERID(YAL)DIY SEYVIG(QSY)KIPDY GRDVIID(SQO)YFTVAPDI	514 515 516 517	0.46 0.38 1.38 3.48	0.88 0.83 1.78 3.42	3.44 4.60 4.60 5.93	3.80 1.30 4.80 4.91	0.87 1.38 2.68 4.88	1.07 0.81 2.82 3.88

Table 4: Sequence and conformational search construction scheme for each of the 24 CDRs, []=construction area, ()=Chain closure, all sidechains are constructed. RMS(Root Mean Square) difference between model and crystal structure loop coordinates. The RMS values are a global fit calculated by least-squares fitting the conserved core of the two structures upon each other and calculating the RMS over the loops. The total RMS of the frameworks (N,Ca,C) is 0.81, 0.60, 0.86 and 0.56 respectively

Loop	Canonical	Sequence	SEQ ID NO
L1	HyHEL-10	R A S Q S I S R W L A	518
	(3D6)	R A S Q S I G N N L H	497
L2	REI	E A S N D L A	519
	(3D6)	K A S S L E S	501
H1	McPC603	D F Y M E	520
	(3D6)	D Y A M H	509
H2	KOL	I I W D D G S D Q	521
	(3D6)	I S W D S S S I G	513

Table 5: Canonical loops selected for the model of 3D6(taken from Chothia *et al* (1989)).

Table 6:

Backbone ϕ and ψ angles of residues in CDR-L1 from HyHEL-10 and REI classified in the same canonical group by Chothia <i>et al</i> (1989). The residues exhibiting a peptide flip are indicated by a *.							
Residue Number		24	25	26	27	28*	29*
REI	Sequence ϕ/ψ	Q -138	A -103/157	S -96/7	Q -158/142	S -40/108	I 112/9
HyHEL-10	Sequence ϕ/ψ	R -108	A -85/135	S -88/64	Q 172/160	S -64/-38	I 9/63
Residue Number		30*	31*	32	33	32	
REI	Sequence ϕ/ψ	I 79/-77	K -146/21	Y -104/89	L -143/133	N -144/-	SEQ ID NO: 522
HyHEL-10	Sequence ϕ/ψ	G -63/107	N 85/-15	N -105/12	L -129/118	H -126/-	SEQ ID NO: 518

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(ix) TELECOMMUNICATION INFORMATION:

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(B) TELEFAX: (202) 293-7860
(C) TELEX: 6491103

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(1) INFORMATION FOR SEQ ID NO:1

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

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(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

EP 0 592 106 B1

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

5 Glu Arg Val Ser Leu Thr Cys Arg Ala Ser Gln Glu Ile Ser Gly Tyr
20 25 30

10 Leu Ser Trp Leu Gln Gln Lys Pro Asp Gly Thr Ile Lys Arg Leu Ile
35 40 45

15 Tyr Ala Ala Ser Thr Leu Asp Ser Gly Val Pro Lys Arg Phe Ser Gly
50 55 60

Arg Arg Ser Gly Ser Asp Tyr Ser Leu Thr Ile Ser Ser Leu Glu Ser
65 70 75 80

20 Glu Asp Phe Ala Asp Tyr Tyr Cys Leu Gln Tyr Leu Ser Tyr Pro Leu
85 90 95

25 Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala
100 105

(2) INFORMATION FOR SEQ ID NO:2

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Asp Ile Gln Met Thr Gln Ser Pro Ala Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Glu Thr Val Thr Ile Thr Cys Arg Ala Ser Gly Asn Ile His Asn Tyr
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Gln Gly Lys Ser Pro Gln Leu Leu Val
35 40 45

Tyr Tyr Thr Thr Thr Leu Ala Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Gln Tyr Ser Leu Lys Ile Asn Ser Leu Gln Pro
65 70 75 80

Glu Asp Phe Gly Ser Tyr Tyr Cys Gln His Phe Trp Ser Thr Pro Arg
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg
100 105

(3) INFORMATION FOR SEQ ID NO:3

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 107 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

EP 0 592 106 B1

Asp Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
 1 5 10 15
 5
 Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Asn Tyr Met
 20 25 30
 10
 Tyr Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr
 35 40 45
 15
 Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Val Arg Phe Ser Gly Ser
 50 55 60
 20
 Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Thr Glu
 65 70 75 80
 25
 Asp Ala Ala Glu Tyr Tyr Cys Gln Gln Trp Gly Arg Asn Pro Thr Phe
 85 90 95
 30
 Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
 100 105

(4) INFORMATION FOR SEQ ID NO:4

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 109 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

Asp Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Val Thr Pro Gly
 1 5 10 15

EP 0 592 106 B1

Asn Ser Val Ser Leu Ser Cys Arg Ala Ser Gln Ser Ile Gly Asn Asn
20 25 30

Leu His Trp Tyr Gln Gln Lys Ser His Glu Ser Pro Arg Leu Leu Ile
35 40 45

Lys Tyr Ala Ser Gln Ser Ile Ser Gly Ile Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Ser Ile Asn Ser Val Glu Thr
65 70 75 80

Glu Asp Phe Gly Met Tyr Phe Cys Gln Gln Ser Asn Ser Trp Pro Tyr
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
100 105

(5) INFORMATION FOR SEQ ID NO:5

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 108 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

Glu Ile Val Leu Thr Gln Ser Pro Ala Ile Thr Ala Ala Ser Leu Gly
1 5 10 15

Gln Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Ser Leu
20 25 30

His Trp Tyr Gln Gln Lys Ser Gly Thr Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Glu Ile Ser Lys Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Asn Thr Met Glu Ala Glu
65 70 75 80

Asp Ala Ala Ile Tyr Tyr Cys Gln Gln Trp Thr Tyr Pro Leu Ile Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg Ala
100 105

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(6) INFORMATION FOR SEQ ID NO:6

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 112 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

20

Glu Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
1 5 10 15

25

Arg Val Thr Ile Ser Cys Thr Gly Thr Ser Ser Asn Ile Gly Ser Ile
20 25 30

Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Met Ala Pro Lys Leu Leu
35 40 45

30

Ile Tyr Arg Asp Ala Met Arg Pro Ser Gly Val Pro Thr Arg Phe Ser
50 55 60

35

Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Glu
65 70 75 80

Ala Glu Asp Glu Ser Asp Tyr Tyr Cys Ala Ser Trp Asn Ser Ser Asp
85 90 95

40

Asn Ser Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu Gly Gln
100 105 110

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(7) INFORMATION FOR SEQ ID NO:7

(i) SEQUENCE CHARACTERISTICS:

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- (A) LENGTH: 115 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

EP 0 592 106 B1

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ser Val Ser Ala Gly
1 5 10 15

Glu Arg Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30

Gly Asn Gln Lys Asn Phe Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Gly Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Asn
85 90 95

Asp His Ser Tyr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Ile
100 105 110

Lys Arg Ala
115

(8) INFORMATION FOR SEQ ID NO:8

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 103 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

Ser Val Leu Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln Arg
 1 5 10 15

Val Thr Ile Ser Cys Thr Gly Ser Ser Ser Asn Ile Gly Ala Gly Asn
 20 25 30

His Val Lys Trp Tyr Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
 35 40 45

Ile Phe His Asn Asn Ala Arg Phe Ser Val Ser Lys Ser Gly Ser Ser
 50 55 60

Ala Thr Leu Ala Ile Thr Gly Leu Gln Ala Glu Asp Glu Ala Asp Tyr
 65 70 75 80

Tyr Cys Gln Ser Tyr Asp Arg Ser Leu Arg Val Phe Gly Gly Gly Thr
 85 90 95

Lys Leu Thr Val Leu Arg Gln
 100

(9) INFORMATION FOR SEQ ID NO:9

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 114 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

EP 0 592 106 B1

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30

Gln Gly Asn Thr Tyr Leu Arg Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Val Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asn Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95

Thr His_Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Ala

(10) INFORMATION FOR SEQ ID NO:10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

EP 0 592 106 B1

Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Val
35 40 45

Tyr Tyr Thr Ser Arg Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu His
65 70 75 80

Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Ser Thr Thr Pro Arg
85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Arg
100 105

(11) INFORMATION FOR SEQ ID NO:11

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 109 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

Asp Ile Gln Met Thr Gln Ile Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15

Asp Arg Val Ser Ile Ser Cys Arg Ala Ser Gln Asp Ile Asn Asn Phe
20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Ile Lys Leu Leu Ile
35 40 45

Tyr Phe Thr Ser Arg Ser Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

EP 0 592 106 B1

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln
65 70 75 80

5 Glu Asp Ile Ala Thr Tyr Phe Cys Gln Gln Gly Asn Ala Leu Pro Arg
85 90 95

10 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
100 105

(12) INFORMATION FOR SEQ ID NO:12

(i) SEQUENCE CHARACTERISTICS:

- 15 (A) LENGTH: 107 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

25 Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly
1 5 10 15

30 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Arg Trp
20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Val Pro Lys Leu Leu Ile
35 40 45

40 Tyr Lys Ala Ser Ser Leu Glu Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80

45 Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser Phe
85 90 95

Gly Pro Gly Thr Lys Val Asp Ile Lys Arg Thr
100 105

50 (13) INFORMATION FOR SEQ ID NO:13

(i) SEQUENCE CHARACTERISTICS:

- 55 (A) LENGTH: 104 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

5 Gln Val Gln Leu Gln Gln Ser Gly Thr Glu Leu Ala Arg Pro Gly Ala
1 5 10 15

Ser Val Arg Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Thr Phe
20 25 30

10 Gly Ile Thr Trp Val Lys Gln Arg Thr Gly Gln Gly Leu Glu Trp Ile
35 40 45

15 Gly Glu Ile Phe Pro Gly Asn Ser Lys Thr Tyr Tyr Ala Glu Arg Phe
50 55 60

20 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Thr Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

25 Ala Arg Glu Ile Arg Tyr Trp Gly
100

(14) INFORMATION FOR SEQ ID NO:14

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 107 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

40 Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15

45 Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Gly Tyr
20 25 30

50 Gly Val Asn Trp Val Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45

Gly Met Ile Trp Gly Asp Gly Asn Thr Asp Tyr Asn Ser Ala Leu Lys
50 55 60

EP 0 592 106 B1

Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80

Lys Met Asn Ser Leu His Thr Asp Asp Thr Ala Arg Tyr Tyr Cys Ala
85 90 95

Arg Glu Arg Asp Tyr Arg Leu Asp Tyr Trp Gly
100 105

(15) INFORMATION FOR SEQ ID NO:15

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 106 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Met Lys Pro Gly Ala Ser
1 5 10 15

Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ser Asp Tyr Trp
20 25 30

Ile Glu Trp Val Lys Gln Arg Pro Gly His Gly Leu Glu Trp Ile Gly
35 40 45

Glu Ile Leu Pro Gly Ser Gly Ser Thr Asn Tyr His Glu Arg Phe Lys
50 55 60

Gly Lys Ala Thr Phe Thr Ala Asp Thr Ser Ser Ser Thr Ala Tyr Met
65 70 75 80

Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Gly Val Tyr Tyr Cys Leu
85 90 95

His Gly Asn Tyr Asp Phe Asp Gly Trp Gly
100 105

(16) INFORMATION FOR SEQ ID NO:16

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 104 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

5 Asp Val Gln Leu Gln Glu Ser Gly Pro Ser Leu Val Lys Pro Ser Gln
1 5 10 15

Thr Leu Ser Leu Thr Cys Ser Val Thr Gly Asp Ser Ile Thr Ser Asp
20 25 30

10 Tyr Trp Ser Trp Ile Arg Lys Phe Pro Gly Asn Arg Leu Glu Tyr Met
35 40 45

15 Gly Tyr Val Ser Tyr Ser Gly Ser Thr Tyr Tyr Asn Pro Ser Leu Lys
50 55 60

Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Tyr Tyr Leu
65 70 75 80

20 Asp Leu Asn Ser Val Thr Thr Glu Asp Thr Ala Thr Tyr Tyr Cys Ala
85 90 95

25 Asn Trp Asp Gly Asp Tyr Trp Gly
100

(17) INFORMATION FOR SEQ ID NO:17

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(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

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(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

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Glu Val Lys Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

45 Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Asp Phe Ser Lys Tyr
20 25 30

50 Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Ile
35 40 45

Gly Glu Ile His Pro Asp Ser Gly Thr Ile Asn Tyr Thr Pro Ser Leu
50 55 60

55

EP 0 592 106 B1

Lys Asp Lys Phe Ile Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

5 Leu Gln Met Ser Lys Val Arg Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85 90 95

10 Ala Arg Leu His Tyr Tyr Gly Tyr Asn Ala Tyr Trp Gly
100 105

(18) INFORMATION FOR SEQ ID NO:18

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 117 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

25 Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

30 Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe Ser Ser Tyr
20 25 30

35 Ala Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ile Ile Trp Asp Asp Gly Ser Asp Gln His Tyr Ala Asp Ser Val
50 55 60

40 Lys Gly Arg Phe Thr Ile Ser Arg Asn Asp Ser Lys Asn Thr Leu Phe
65 70 75 80

45 Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

Ala Arg Asp Gly Gly His Gly Phe Cys Ser Ser Ala Ser Cys Phe Gly
100 105 110

50 Pro Asp Tyr Trp Gly
115

55 (19) INFORMATION FOR SEQ ID NO:19

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 113 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

Glu Val Lys Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15
 Ser Leu Arg Leu Ser Cys Ala Thr Ser Gly Phe Thr Phe Ser Asp Phe
 20 25 30
 Tyr Met Glu Trp Val Arg Gln Pro Pro Gly Lys Arg Leu Glu Trp Ile
 35 40 45
 Ala Ala Ser Arg Asn Lys Gly Asn Lys Tyr Thr Thr Glu Tyr Ser Ala
 50 55 60
 Ser Val Lys Gly Arg Phe Ile Val Ser Arg Asp Thr Ser Gln Ser Ile
 65 70 75 80
 Leu Tyr Leu Gln Met Asn Ala Leu Arg Ala Glu Asp Thr Ala Ile Tyr
 85 90 95
 Tyr Cys Ala Arg Asn Tyr Tyr Gly Ser Thr Trp Tyr Phe Asp Val Trp
 100 105 110
 Gly

(20) INFORMATION FOR SEQ ID NO:20

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 107 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

Val Gln Leu Glu Gln Ser Gly Pro Gly Leu Val Arg Pro Ser Gln Thr
 1 5 10 15
 Leu Ser Leu Thr Cys Thr Val Ser Gly Thr Ser Phe Asp Asp Tyr Tyr
 20 25 30

EP 0 592 106 B1

Ser Thr Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly
35 40 45

Tyr Val Phe Tyr His Gly Thr Ser Asp Thr Asp Thr Pro Leu Arg Ser
50 55 60

Arg Val Thr Met Leu Val Asn Thr Ser Lys Asn Gln Phe Ser Leu Arg
65 70 75 80

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala Arg
85 90 95

Asn Leu Ile Ala Gly Cys Ile Asp Val Trp Gly
100 105

(21) INFORMATION FOR SEQ ID NO:21

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 109 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

Glu Val Lys Leu Asp Glu Thr Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Pro Met Lys Leu Ser Cys Val Ala Ser Gly Phe Thr Phe Ser Asp Tyr
20 25 30

Trp Met Asn Trp Val Arg Gln Ser Pro Glu Lys Gly Leu Glu Trp Val
35 40 45

Ala Gln Ile Arg Asn Lys Pro Tyr Asn Tyr Glu Thr Tyr Tyr Ser Asp
50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Ser Lys Ser Ser
65 70 75 80

Val Tyr Leu Gln Met Asn Asn Leu Arg Val Glu Asp Met Gly Ile Tyr
85 90 95

Tyr Cys Thr Gly Ser Tyr Tyr Gly Met Asp Tyr Trp Gly
100 105

(22) INFORMATION FOR SEQ ID NO:22

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 115 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

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10  Gln Val Gln Leu Lys Glu Ser Gly Ala Glu Leu Val Ala Ala Ser Ser
    1           5           10           15

15  Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
    20           25           30

20  Gly Val Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
    35           40           45

25  Gly Tyr Ile Asn Pro Gly Lys Gly Tyr Leu Ser Tyr Asn Glu Lys Phe
    50           55           60

30  Lys Gly Lys Thr Thr Leu Thr Val Asp Arg Ser Ser Ser Thr Ala Tyr
    65           70           75           80

    Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
    85           90           95

35  Ala Arg Ser Phe Tyr Gly Gly Ser Asp Leu Ala Val Tyr Tyr Phe Asp
    100          105          110

    Ser Trp Gly
    115

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(23) INFORMATION FOR SEQ ID NO:23

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

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50  Glu Val Gln Leu Gln Gln Ser Gly Val Glu Leu Val Arg Ala Gly Ser
    1           5           10           15

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EP 0 592 106 B1

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Asn
20 25 30

Gly Ile Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45

Gly Tyr Asn Asn Pro Gly Asn Gly Tyr Ile Ala Tyr Asn Glu Lys Phe
50 55 60

Lys Gly Lys Thr Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
85 90 95

Ala Arg Ser Glu Tyr Tyr Gly Gly Ser Tyr Lys Phe Asp Tyr Trp Gly
100 105 110

(24) INFORMATION FOR SEQ ID NO:24

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 117 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Asn Asp Tyr
20 25 30

Ala Met⁻His⁻ Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Gly Ile Ser Trp Asp Ser Ser Ser Ile Gly Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Met Ala Leu Tyr Tyr Cys
85 90 95

EP 0 592 106 B1

Val Lys Gly Arg Asp Tyr Tyr Asp Ser Gly Gly Tyr Phe Thr Val Ala
100 105 110

Phe Asp Ile Trp Gly
115

(25) INFORMATION FOR SEQ ID NO:25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 111 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ile Ile Ile His Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Glu Trp Phe Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Met Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

(26) INFORMATION FOR SEQ ID NO:26

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 110 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

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Gln Ser Val Leu Thr Gln Pro Pro Ser Ala Ser Gly Thr Pro Gly Gln
 Arg Val Thr Ile Ser Cys Ser Gly Thr Ser Ser Asn Ile Gly Ser Ser
 Thr Val Asn Trp Tyr Gln Gln Leu Pro Gly Met Ala Pro Lys Leu Leu
 Ile Tyr Arg Asp Ala Met Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
 Gly Ser Lys Ser Gly Ala Ser Ala Ser Leu Ala Ile Gly Gly Leu Gln
 Ser Glu Asp Glu Thr Asp Tyr Tyr Cys Ala Ala Trp Asp Val Ser Leu
 Asn Ala Tyr Val Phe Gly Thr Gly Thr Lys Val Thr Val Leu

(27) INFORMATION FOR SEQ ID NO:27

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 111 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

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Gln Val Leu Met Thr Gln Thr Pro Ser Ser Leu Pro Val Thr Leu Gly
 Gln Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ile Ile Ile His Ser
 Asp Gly Asn Thr Tyr Leu Glu Trp Phe Leu Gln Lys Pro Gly Gln Ser
 Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
 Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Ser Phe Thr Leu Ala Ile

Ser Arg Val Glu Ala Glu Asp Glu Gly Val Tyr Tyr Cys Phe Gln Gly
 85 90 95

Ser His Val Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
 100 105 110

(28) INFORMATION FOR SEQ ID NO:28

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

Asp Val Val Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
 1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val Tyr Ser
 20 25 30

Asp Gly Asn Thr Tyr Leu Asn Trp Phe Gln Gln Arg Pro Gly Gln Ser
 35 40 45

Pro Arg Arg Leu Ile Tyr Lys Val Ser Asn Arg Asp Ser Gly Val Pro
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Met Gln Gly
 85 90 95

Thr His Trp Ser Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105 110

(29) INFORMATION FOR SEQ ID NO:29

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 111 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

EP 0 592 106 B1

Asp Val Leu Met Thr Gln Ser Pro Leu Ser Leu Pro Val Thr Leu Gly
1 5 10 15

Gln Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ile Ile Ile His Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Glu Trp Phe Gln Gln Arg Pro Gly Gln Ser
35 40 45

Pro Arg Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro His Thr Phe Gly Gly Gly Thr Lys Val Glu Ile
100 105 110

(30) INFORMATION FOR SEQ ID NO:30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 112 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Ala Val Ser Leu Gly
1 5 10 15

Glu Arg Ala Thr Ile Asn Cys Lys Ser Ser Gln Ser Val Leu Tyr Ser
20 25 30

Ser Asn Asn Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45

Pro Pro Lys Leu Leu Ile Tyr Trp Ala Ser Thr Arg Glu Ser Gly Val
50 55 60

Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80

EP 0 592 106 B1

Ile Ser Ser Leu Gln Ala Glu Asp Val Ala Val Tyr Tyr Cys Gln Gln
85 90 95

Tyr Asp Thr Ile Pro Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
100 105 110

(31) INFORMATION FOR SEQ ID NO:31

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 111 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

Asp Val Leu Met Thr Gln Thr Pro Asp Ser Leu Pro Val Ser Leu Gly
1 5 10 15

Asp Arg Ala Ser Ile Ser Cys Arg Ser Ser Gln Ile Ile Ile His Ser
20 25 30

Asp Gly Asn Thr Tyr Leu Glu Trp Phe Leu Gln Lys Pro Gly Gln Ser
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Met Ile
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95

Ser His Val Pro His Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

(32) INFORMATION FOR SEQ ID NO:32

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 117 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

EP 0 592 106 B1

Asp Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Arg Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Glu Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Gly Ser Phe Thr Ile Tyr His Ala Asp Thr Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Pro Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Thr Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Met Arg Lys Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser
115

(33) INFORMATION FOR SEQ ID NO:33

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 125 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

Glu Val Gln Leu Val Gln Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ser Ser Ser Gly Phe Ile Phe Ser Ser Tyr
20 25 30

Ala Met Tyr Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Ile Ile Trp Asp Asp Gly Ser Asp Gln His Tyr Ala Asp Ser Val
50 55 60

EP 0 592 106 B1

Lys Gly Arg Phe Thr Ile Ser Arg Asn Asp Ser Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Asp Ser Leu Arg Pro Glu Asp Thr Gly Val Tyr Phe Cys
85 90 95

Ala Arg Asp Gly Gly His Gly Phe Cys Ser Ser Ala Ser Cys Phe Gly
100 105 110

Pro Asp Tyr Trp Gly Gln Gly Thr Pro Val Thr Val Ser
115 120 125

(34) INFORMATION FOR SEQ ID NO:34

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 117 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ile Phe Ser Ser Phe
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Asp Gly Phe Thr Ile Tyr His Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asp Pro Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Thr Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Met Arg Lys Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser
115

(35) INFORMATION FOR SEQ ID NO:35

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 120 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45
Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Asp Arg Lys Asp Trp Gly Trp Ala Leu Phe Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Leu Val Thr Val Ser
115 120

(36) INFORMATION FOR SEQ ID NO:36

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 117 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
 20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Tyr Ile Ser Ser Gly Ser Phe Thr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Met Arg Lys Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
 100 105 110

Leu Val Thr Val Ser
 115

(37) INFORMATION FOR SEQ ID NO:37

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 98 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

Trp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Asn Ile Lys Gln Asp Gly Ser Glu Lys Tyr Tyr Val Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg

(38) INFORMATION FOR SEQ ID NO:38

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 117 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Phe
20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Gly Ser Phe Thr Ile Tyr His Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Phe
65 70 75 80

Leu Gln Met Thr Ser Leu Arg Ala Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95

Ala Arg Met Arg Lys Gly Tyr Ala Met Asp Tyr Trp Gly Gln Gly Thr
100 105 110

Thr Val Thr Val Ser
115

(39) INFORMATION FOR SEQ ID NO:39

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

5 Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr
 1 5 10 15

(40) INFORMATION FOR SEQ ID NO:40

10 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

20

Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Asp Tyr Glu Lys Lys
 1 5 10 15

25

(41) INFORMATION FOR SEQ ID NO:41

(i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

35

Lys Thr Ser Leu Arg Pro Gly Lys Gly Ser Ser Glu Tyr Glu Lys Lys
 1 5 10 15

40

(42) INFORMATION FOR SEQ ID NO:42

(i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

50

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp His Glu Lys Lys
 1 5 10 15

55

EP 0 592 106 B1

(43) INFORMATION FOR SEQ ID NO:43

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

15 Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys
1 5 10 15

(44) INFORMATION FOR SEQ ID NO:44

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

30

Gln Ser Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys
1 5 10 15

35

(45) INFORMATION FOR SEQ ID NO:45

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

50 Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Lys
1 5 10 15

55

(46) INFORMATION FOR SEQ ID NO:46

(i) SEQUENCE CHARACTERISTICS:

55

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

5

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glx Lys Lys
1 5 10 15

(47) INFORMATION FOR SEQ ID NO:47

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

20

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Pro Glu Lys Thr
1 5 10 15

25

(48) INFORMATION FOR SEQ ID NO:48

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

35

Gln Thr Ser Leu Arg Ala Asp Lys Gly Ser Ser Asp Gln Glu Lys Lys
1 5 10 15

40

(49) INFORMATION FOR SEQ ID NO:49

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

50

Gln Thr Ser Leu Arg Pro Asp Lys Gly Lys Ser Asp Ser Glu Lys Lys
1 5 10 15

55

(50) INFORMATION FOR SEQ ID NO:50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

Gln Thr Ser Leu Arg Pro Ala Arg Gly Ser Ser Asp Gln Glu Lys Lys
1 5 10 15

(51) INFORMATION FOR SEQ ID NO:51

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

Gln Thr Ser Leu Lys Pro Gly Arg Gly Ser Ser Asp Pro Glu Lys Lys
1 5 10 15

(52) INFORMATION FOR SEQ ID NO:52

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

Gln Thr Ser Leu Arg Pro Gly Arg Gly Ser Ser Asp Thr Glu Lys Lys
1 5 10 15

(53) INFORMATION FOR SEQ ID NO:53

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

5 Gln Ile_Ser_ Leu Arg Pro Gly Lys Gly Ser Ser Asp Ser Glu Lys Lys
 1 5 10 15

(54) INFORMATION FOR SEQ ID NO:54

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

20 Gln Thr Ser Leu Arg Pro Gly Lys Gly Asp Ser Asp Glu Asp Lys Lys
 1 5 10 15

(55) INFORMATION FOR SEQ ID NO:55

25

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

30

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

35

 Glu Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Ala Asp Lys Lys
 1 5 10 15

40

(56) INFORMATION FOR SEQ ID NO:56

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

55 Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Lys Lys
 1 5 10 15

(57) INFORMATION FOR SEQ ID NO:57

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Glu Lys Lys
1 5 10 15

(58) INFORMATION FOR SEQ ID NO:58

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asx Ala Asx Lys Lys
1 5 10 15

(59) INFORMATION FOR SEQ ID NO:59

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

Val Thr Ala Leu Arg Pro Gly Lys Gly Ala Ser Asp Glu Asp Asp Glu
1 5 10 15

(60) INFORMATION FOR SEQ ID NO:60

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

Gln Thr Ser Leu Arg Pro Asp Lys Gly Ser Ser Asp Gln Glu Thr Thr
1 5 10 15

(61) INFORMATION FOR SEQ ID NO:61

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

Gln Asn Ser Leu Thr Pro Gly Lys Gly Ser Ser Ser Pro Glu Lys Lys
1 5 10 15

(62) INFORMATION FOR SEQ ID NO:62

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ser Asp Lys Lys
1 5 10 15

(63) INFORMATION FOR SEQ ID NO:63

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(64) INFORMATION FOR SEQ ID NO:64

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

10 Val Thr Arg Val Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(65) INFORMATION FOR SEQ ID NO:65

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

25 Leu Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ser Glu Lys Lys
1 5 10 15

30 (66) INFORMATION FOR SEQ ID NO:66

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

45 Val Thr Lys Val Arg Pro Gly Lys Gly Asp Ser Asp Ser Glu Gln Lys
1 5 10 15

(67) INFORMATION FOR SEQ ID NO:67

50 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

EP 0 592 106 B1

Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(68) INFORMATION FOR SEQ ID NO:68

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

Val Thr Lys Val Arg Pro Glu Lys Gly Asp Ser Asp Ser Glu Lys Lys
1 5 10 15

(69) INFORMATION FOR SEQ ID NO:69

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

Val Thr Lys Val Ser Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(70) INFORMATION FOR SEQ ID NO:70

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

Val Thr Lys Val Arg Ser Gly Lys Gly Glu Ser Asp Ala Glu Lys Lys
1 5 10 15

(71) INFORMATION FOR SEQ ID NO:71

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

10 Val Thr Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(72) INFORMATION FOR SEQ ID NO:72

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

25 Val Ser Ser Val Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(73) INFORMATION FOR SEQ ID NO:73

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

40 Val Thr Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

45 (74) INFORMATION FOR SEQ ID NO:74

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

EP 0 592 106 B1

Val Ser Ser Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

5 (75) INFORMATION FOR SEQ ID NO:75

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Val Thr Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

20

(76) INFORMATION FOR SEQ ID NO:76

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

35 Val Ser Pro Ala Lys Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

40 (77) INFORMATION FOR SEQ ID NO:77

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Val Thr Lys Ala Arg Pro Gly Lys Gly Asp Ser Asp Val Glu Lys Asn
1 5 10 15

55 (78) INFORMATION FOR SEQ ID NO:78

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

10 Val Thr Leu Ile Pro Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(79) INFORMATION FOR SEQ ID NO:79

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

25 Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(80) INFORMATION FOR SEQ ID NO:80

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

40 Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Asp Lys Lys
1 5 10 15

45 (81) INFORMATION FOR SEQ ID NO:81

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

EP 0 592 106 B1

Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Arg Lys
1 5 10 15

5

(82) INFORMATION FOR SEQ ID NO:82

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

Val Thr Leu Leu Gln Ala Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

20

(83) INFORMATION FOR SEQ ID NO:83

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

35

Val Thr Leu Leu Gln Pro Gly Glu Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

40

(84) INFORMATION FOR SEQ ID NO:84

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

Leu Thr Leu Leu Gln Pro Gly Asn Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

55

(85) INFORMATION FOR SEQ ID NO:85

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

Val Thr Leu Leu Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Ile
1 5 10 15

(86) INFORMATION FOR SEQ ID NO:86

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

Val Thr Leu Phe Gln Pro Gly Gln Gly Asp Ser Asp Pro Glu Lys Lys
1 5 10 15

(87) INFORMATION FOR SEQ ID NO:87

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
1 5 10 15

(88) INFORMATION FOR SEQ ID NO:88

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

5 Val Thr Leu Pro Gln Pro Gly Lys Gly Asp Trp Asp Ala Glu Lys Lys
 1 5 10 15

(89) INFORMATION FOR SEQ ID NO:89

10 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

15

 (ii) MOLECULE TYPE: peptide

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

20

 Val Thr Phe Leu Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys
 1 5 10 15

25

(90) INFORMATION FOR SEQ ID NO:90

 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

30

 (ii) MOLECULE TYPE: peptide

35

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

40

 Glu Ser Ser Ala Arg Pro Gly Lys Gly Asp Ser Asp Ala Glu Lys Lys
 1 5 10 15

(91) INFORMATION FOR SEQ ID NO:91

45 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

50

 (ii) MOLECULE TYPE: peptide

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

55

 Val Thr Leu Ser Ser Pro Gly Gln Gly Asp Ser Asp Ala Glu Lys Lys
 1 5 10 15

EP 0 592 106 B1

(92) INFORMATION FOR SEQ ID NO:92

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

15 Val Thr Thr Ala Lys Pro Glu Lys Gly Asp Ser Asp Val Glu Lys Lys
1 5 10 15

(93) INFORMATION FOR SEQ ID NO:93

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

30

Val Thr Thr Pro Lys Pro Asp Lys Gly Asp Ser Asp Val Glu Lys Lys
1 5 10 15

(94) INFORMATION FOR SEQ ID NO:94

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

45

Val Thr Ala Pro Arg Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
1 5 10 15

50

(95) INFORMATION FOR SEQ ID NO:95

(i) SEQUENCE CHARACTERISTICS:

55 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

5
Val Thr Ala Pro Lys Pro Gly Lys Gly Thr Ser Ser Ala Glu Lys Lys
1 5 10 15

10 (96) INFORMATION FOR SEQ ID NO:96

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

25 Val Thr Thr Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
1 5 10 15

(97) INFORMATION FOR SEQ ID NO:97

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

40 Val Ser Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
1 5 10 15

(98) INFORMATION FOR SEQ ID NO:98

45 (i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

55

Val Thr Ala Pro Arg Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
 1 5 10 15

5

(99) INFORMATION FOR SEQ ID NO:99

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Val Thr Ala Pro Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
 1 5 10 15

20

(100) INFORMATION FOR SEQ ID NO:100

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

Val Thr Ala Pro Lys Pro Asp Lys Gly Val Ser Ser Ala Glu Lys Lys
 1 5 10 15

35

(101) INFORMATION FOR SEQ ID NO:101

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

Val Thr Ala Pro Lys Ser Glu Lys Gly Val Ser Ser Ala Glu Lys Lys
 1 5 10 15

50

(102) INFORMATION FOR SEQ ID NO:102

(i) SEQUENCE CHARACTERISTICS:

55

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) _MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

10 **Phe Thr Ala Pro Lys Pro Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys**
1 5 10 15

(103) INFORMATION FOR SEQ ID NO:103

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

25 **Leu Thr Ala Pro Lys Pro Gly Arg Gly Val Ser Ser Ala Glu Lys Lys**
1 5 10 15

30 (104) INFORMATION FOR SEQ ID NO:104

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

35 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Val Thr Ala Pro Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Arg
1 5 10 15

45 (105) INFORMATION FOR SEQ ID NO:105

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

EP 0 592 106 B1

Val Ser Ala Pro Lys Pro Gly Lys Glu Gly Ser Ser Ala Glu Lys Lys
1 5 10 15

(106) INFORMATION FOR SEQ ID NO:106

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

Val Thr Ala Pro Lys Pro Arg Lys Gly Ala Ser Ser Ala Glu Lys Lys
1 5 10 15

(107) INFORMATION FOR SEQ ID NO:107

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Ala Glu Leu Pro
1 5 10 15

(108) INFORMATION FOR SEQ ID NO:108

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

Val Thr Phe Leu Ser Pro Gly Gln Gly Asn Ser Asp Glu Asp Leu Pro
1 5 10 15

(109) INFORMATION FOR SEQ ID NO:109

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

10 **Val Thr Leu Ser Ser Pro Gln Arg Gly Asp Ser Asp Ala Glu Lys Lys**
1 5 10 15

(110) INFORMATION FOR SEQ ID NO:110

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

25

Val Thr Ala Pro Lys Ser Ser Lys Gly Gly Ser Ser Ala Glu Lys Lys
1 5 10 15

30

(111) INFORMATION FOR SEQ ID NO:111

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:111:

45 **Gln Thr Ser Pro Thr Pro Gly Lys Gly Ser Ser Asp Pro Glu Lys Lys**
1 5 10 15

(112) INFORMATION FOR SEQ ID NO:112

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:112:

Gln Ile Ser Leu Ile Pro Gly Lys Gly Ser Tyr Asp Asp Glu Lys Lys
1 5 10 15

5

(113) INFORMATION FOR SEQ ID NO:113

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:

Val Thr Ala Leu Lys Ser Gly Lys Gly Ala Ser Ser Ala Glu Lys Lys
1 5 10 15

20

(114) INFORMATION FOR SEQ ID NO:114

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:114:

Val Thr Ala Leu Lys Ser Asp Lys Gly Ala Ser Ser Gly Glu Lys Lys
1 5 10 15

35

(115) INFORMATION FOR SEQ ID NO:115

40

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:115:

50

Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Ala Glu Lys Lys
1 5 10 15

55

(116) INFORMATION FOR SEQ ID NO:116

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:116:

10 Val Thr Pro Pro Ser Pro Gly Gln Gly Asp Ser Ala Arg Glu Lys Lys
1 5 10 15

(117) INFORMATION FOR SEQ ID NO:117

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:117:

25

Val Thr Val Arg Lys Pro Gly Lys Gly Asp Ser Ser Asp Glu Lys Lys
1 5 10 15

(118) INFORMATION FOR SEQ ID NO:118

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

35 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:118:

40

Gln Thr Ser Val Arg Leu Gly Gln Gly Ser Ser Asp Pro Glu Lys Lys
1 5 10 15

45

(119) INFORMATION FOR SEQ ID NO:119

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:119:

55

EP 0 592 106 B1

Lys Thr Ser Leu Arg Pro Trp Lys Gly Ser Ser Asp Ser Asp Lys Lys
1 5 10 15

(120) INFORMATION FOR SEQ ID NO:120

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:120:

Gln Thr Asp Val Thr Gln Gly Gln Gly Ser Ser Gln Pro Glu Lys Lys
1 5 10 15

(121) INFORMATION FOR SEQ ID NO:121

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:121:

Gln Thr Ala Val Ser Gln Gly Gln Gly Ser Ser Gln Ser Glu Lys Lys
1 5 10 15

(122) INFORMATION FOR SEQ ID NO:122

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Leu Thr Ala Pro Arg Thr Asn Arg Gly Ser Ser Asp Ser Glu Lys Lys
1 5 10 15

(123) INFORMATION FOR SEQ ID NO:123

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

Val Thr Ala Pro Ser Ser His Arg Gly Ser Ser Asp Thr Glu Lys Lys
1 5 10 15

(124) INFORMATION FOR SEQ ID NO:124

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:124:

Leu Leu Ser Leu Ser Pro Leu Lys Gly Asp Ser Asp Pro Glu Lys Val
1 5 10 15

(125) INFORMATION FOR SEQ ID NO:125

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125:

Val Thr Ala Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu
1 5 10 15

(126) INFORMATION FOR SEQ ID NO:126

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:126:

Val Thr Ile Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu
1 5 10 15

(127) INFORMATION FOR SEQ ID NO:127

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:127:

Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu
1 5 10 15

(128) INFORMATION FOR SEQ ID NO:128

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:128:

Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Lys Leu
1 - - 5 10 15

(129) INFORMATION FOR SEQ ID NO:129

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:129:

Ala Val Ser Pro Thr Pro Asp Thr Gly Val Ile Lys Thr Glu Lys Leu
1 5 10 15

(130) INFORMATION FOR SEQ ID NO:130

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130:

Ala Val Ser Pro Thr Pro Asp Thr Gly Ala Ile Lys Thr Glu Pro Ser
1 5 10 15

10

(131) INFORMATION FOR SEQ ID NO:131

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:131:

Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Lys Leu
1 5 10 15

25

(132) INFORMATION FOR SEQ ID NO:132

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:132:

40

Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Met Arg Leu
1 5 10 15

(133) INFORMATION FOR SEQ ID NO:133

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:

55

Tyr Leu Pro Pro Thr Pro Gly Leu Ile Arg Ser Thr Ser Met Lys Leu
1 5 10 15

(134) INFORMATION FOR SEQ ID NO:134

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134:

Tyr Leu Pro Pro Thr Pro Gly Leu Ile Arg Ser Thr Ser Val Lys Leu
1 5 10 15

(135) INFORMATION FOR SEQ ID NO:135

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:135:

Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

(136) INFORMATION FOR SEQ ID NO:136

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:136:

Tyr Leu Pro Pro Thr Pro Gly Val Ile Arg Ser Thr Ala Gly Lys Leu
1 5 10 15

(137) INFORMATION FOR SEQ ID NO:137

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:137:

10 Tyr Leu Pro Ala Thr Pro Gly Val Val Arg Ser Ser Ala Gly Met Leu
1 5 10 15

(138) INFORMATION FOR SEQ ID NO:138

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:138:

25 Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

(139) INFORMATION FOR SEQ ID NO:139

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:139:

40 Ser Leu Pro Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asn Lys Leu
1 5 10 15

45 (140) INFORMATION FOR SEQ ID NO:140

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:140:

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Lys Leu
1 5 10 15

5

(141) INFORMATION FOR SEQ ID NO:141

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 16 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:141:

20

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Asp Lys Leu
1 5 10 15

(142) INFORMATION FOR SEQ ID NO:142

25

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

35

Ser Leu Pro Pro Arg Pro Gly Arg Val Arg Ser Ser Ser Glu Lys Leu
1 5 10 15

40

(143) INFORMATION FOR SEQ ID NO:143

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 16 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

50

Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Gln Leu
1 5 10 15

55

(144) INFORMATION FOR SEQ ID NO:144

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:144:

10 Ser Leu Pro Pro Arg Pro Gly Lys Val Arg Ser Ser Ser Glu Thr Leu
1 5 10 15

(145) INFORMATION FOR SEQ ID NO:145

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:145:

25 Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Lys Leu
1 5 10 15

30 (146) INFORMATION FOR SEQ ID NO:146

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

35 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:146:

45 Ser Leu Pro Pro Lys Pro Gly Arg Ile Arg Ser Ser Thr Gly Lys Leu
1 5 10 15

(147) INFORMATION FOR SEQ ID NO:147

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:147:

Ser Leu Pro Pro Lys Pro Gly Lys Ile Arg Ser Ser Thr Gly Gln Leu
1 5 10 15

5

(148) INFORMATION FOR SEQ ID NO:148

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:148:

Ser Leu Pro Pro Glu Pro Gly Lys Ile Arg Ser Ser Thr Gly Arg Leu
1 5 10 15

20

(149) INFORMATION FOR SEQ ID NO:149

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:

Ser Leu Ala Pro Ser Pro Gly Lys Ile Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

35

(150) INFORMATION FOR SEQ ID NO:150

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:

Ser Leu Pro Pro Arg Pro Gly Lys Ile Arg Ser Ser Thr Gly Asn Val
1 5 10 15

55

(151) INFORMATION FOR SEQ ID NO:151

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

- 5 (ii) MOLECULE TYPE: peptide
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:151:

10 **Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu**
1 5 10 15

(152) INFORMATION FOR SEQ ID NO:152

- 15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

- 20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:152:

25 **Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Asp Lys Leu**
1 5 10 15

(153) INFORMATION FOR SEQ ID NO:153

- 30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

35 (C) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:

40 **Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Asn Leu**
1 5 10 15

(154) INFORMATION FOR SEQ ID NO:154

- (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

50 (B) TYPE: amino acid

(C) TOPOLOGY: linear

- (ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

Ser Leu Arg Pro Ser Pro Gly Lys Val Arg Ser Ala Val Glu Lys Leu
 1 5 10 15

(155) INFORMATION FOR SEQ ID NO:155

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:155:

Ser Leu Pro Pro Arg Pro Gly Lys Arg Ser Ser Ala Glu Lys Leu
 1 5 10 15

(156) INFORMATION FOR SEQ ID NO:156

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:156:

Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Val Glu Arg Leu
 1 5 10 15

(157) INFORMATION FOR SEQ ID NO:157

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:157:

Ser Leu Ala Pro Ser Pro Asp Lys Ile Arg Ser Thr Pro Asp Lys Leu
 1 5 10 15

(158) INFORMATION FOR SEQ ID NO:158

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:158:

10 Ser Leu Ala Leu Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

(159) INFORMATION FOR SEQ ID NO:159

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:159:

25 Ser Leu Pro Leu Ser Ala Gly Lys Val Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

30 (160) INFORMATION FOR SEQ ID NO:160

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

35 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:

Ser Leu Ala Pro Ser Pro Gly Lys Val Arg Ser Thr Ala Glu Tyr Leu
1 5 10 15

45 (161) INFORMATION FOR SEQ ID NO:161

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:

EP 0 592 106 B1

Ser Leu Pro Leu Thr Pro Gly Leu Ile Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

5 (162) INFORMATION FOR SEQ ID NO:162

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:162:

Ser Leu Pro Leu Thr Pro Arg Val Ile Arg Ser Thr Ala Glu Lys Leu
1 5 10 15

20 (163) INFORMATION FOR SEQ ID NO:163

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:163:

Phe Leu His Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Lys Leu
1 5 10 15

(164) INFORMATION FOR SEQ ID NO:164

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

50 Phe Leu Leu Pro Thr Pro Gly Thr Asp Ser Ser Ser Thr Glu Arg Leu
1 5 10 15

55 (165) INFORMATION FOR SEQ ID NO:165

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

10 Phe Leu His Pro Thr Arg Val Thr Asp Ser Ser Ser Thr Glu Lys Leu
1 5 10 15

(166) INFORMATION FOR SEQ ID NO:166

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:166:

25

Leu Leu Pro Pro Thr Pro Gly Thr Asn Ser Ser Ser Asn Asp Lys Leu
1 5 10 15

30

(167) INFORMATION FOR SEQ ID NO:167

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:

45 Val Leu Pro Leu Ser Pro His Arg Ile Arg Ser Glu Ser Glu Asn Leu
1 5 10 15

(168) INFORMATION FOR SEQ ID NO:168

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Ser Leu Ala Pro Ser Pro Ala Lys Phe Arg Ser Thr Ala Glu Arg Asp
 1 5 10 15

5 (169) INFORMATION FOR SEQ ID NO:169

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:169:

Val Thr Ala Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys
 1 5 10 15

20

(170) INFORMATION FOR SEQ ID NO:170

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

30 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:170:

Val Thr Ala Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys
 1 5 10 15

35

(171) INFORMATION FOR SEQ ID NO:171

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 16 amino acids
 (B) TYPE: amino acid
 45 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

50

Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys
 1 5 10 15

55

(172) INFORMATION FOR SEQ ID NO:172

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172:

10 Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Asp Lys Lys
1 5 10 15

(173) INFORMATION FOR SEQ ID NO:173

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:173:

25

Val Thr Gly Pro Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Lys Lys
1 5 10 15

(174) INFORMATION FOR SEQ ID NO: 174

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:

40

Val Thr Gly Pro Arg Pro Gly Arg Ile Arg Ser Asp Pro Xaa Lys Lys
1 5 10 15

45

(175) INFORMATION FOR SEQ ID NO:175

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

55

EP 0 592 106 B1

Val Thr Ala Pro Arg Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys
1 5 10 15

5 (176) INFORMATION FOR SEQ ID NO:176

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:176:

Val Thr Gly Pro Ser Arg Gly Arg Ile Arg Ser Asp Pro Glu Lys Lys
1 5 10 15

20 (177) INFORMATION FOR SEQ ID NO:177

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:177:

Val Thr Val Pro Arg Pro Ser Arg Ile Arg Ser Glu Ser Glu Arg Lys
1 5 10 15

35 (178) INFORMATION FOR SEQ ID NO:178

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

50 Val Thr Ala Pro Gly Pro Gly Arg Ile Arg Ser Glu Ser Glu Arg Lys
1 5 10 15

(179) INFORMATION FOR SEQ ID NO:179

55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:179:

Gln Thr Ser Val Arg Pro Gly Arg Val Arg Ser Asp Pro Glu Arg Lys
1 5 10 15

(180) INFORMATION FOR SEQ ID NO:180

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:180:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Arg Lys
1 5 10 15

(181) INFORMATION FOR SEQ ID NO:181

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:181:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Lys
1 5 10 15

(182) INFORMATION FOR SEQ ID NO:182

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:182:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Pro Glu Lys Lys
1 5 10 15

EP 0 592 106 B1

(183) INFORMATION FOR SEQ ID NO:183

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:183:

15 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Pro Asp Lys Lys
1 5 10 15

(184) INFORMATION FOR SEQ ID NO:184

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 **(ii) MOLECULE TYPE: peptide**

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:184:

30 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ala Glu Pro Glu Lys Lys
1 5 10 15

(185) INFORMATION FOR SEQ ID NO:185

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:185:

45 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asx Pro Glx Lys Lys
1 5 10 15

(186) INFORMATION FOR SEQ ID NO:186

(i) SEQUENCE CHARACTERISTICS:

50 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

5 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Asx Lys Lys
 1 5 10 15

(187) INFORMATION FOR SEQ ID NO:187

10 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:

20
Gln Thr Ser Val Arg Pro Gly Gln Val Arg Ser Asp Pro Glu Arg Lys
1 5 10 15

25 (188) INFORMATION FOR SEQ ID NO:188

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

30 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser His Pro Glu Lys Lys
1 5 10 15

(189) INFORMATION FOR SEQ ID NO:189

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50 (ii) MOLECULE TYPE: peptide

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

55 Gln Thr Ser Val Arg Pro Gly Asn Val Arg Ser Asp Pro Asp Lys Lys
 1 5 10 15

EP 0 592 106 B1

(190) INFORMATION FOR SEQ ID NO:190

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:190:

15 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Thr
1 5 10 15

(191) INFORMATION FOR SEQ ID NO:191

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:191:

30 Gln Thr Ser Val Arg Pro Gly Thr Val Arg Ser Glu Pro Glu Lys Lys
1 5 10 15

(192) INFORMATION FOR SEQ ID NO:192

(i) SEQUENCE CHARACTERISTICS:

35

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

45

Gln Thr Ser Val Arg Pro Glu Lys Val Arg Ser Glu Pro Asp Lys Lys
1 5 10 15

(193) INFORMATION FOR SEQ ID NO:193

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

5 Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Glu Ser Asp Lys Lys
 1 5 10 15

(194) INFORMATION FOR SEQ ID NO:194

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

15 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:194:

²⁰

Gln Thr Ser Val Arg Pro Gly Glu Val Arg Ser Glu Pro Asp Lys Lys
1 5 10 15

(195) INFORMATION FOR SEQ ID NO:195

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:195:

35

Gln Thr Ser Val Arg Pro Gly Asx Val Arg Ser Asx Pro Glx Arg Lys
1 5 10 15

(196) INFORMATION FOR SEQ ID NO:196

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:

Gln Thr Ser Val Ser Pro Gly Lys Val Arg Ser Asp Pro Glu Lys Lys
1 5 10 15

55 (197) INFORMATION FOR SEQ ID NO:197

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:197:

10 Gln Thr Ser Val Arg Pro Gly Lys Val Asn Ser Asp Pro Glu Lys Lys
1 5 10 15

(198) INFORMATION FOR SEQ ID NO:198

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:198:

25

Gln Thr Ser Val Arg Pro Gly Lys Val Arg Ser Asp Pro Asp Thr Lys
1 5 10 15

30 (199) INFORMATION FOR SEQ ID NO:199

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
35 (B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:199:

40

Gln Thr Ser Val Arg Pro Lys Lys Val Arg Ser Asp Pro Glx Lys Lys
1 5 10 15

45

(200) INFORMATION FOR SEQ ID NO:200

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
50 (B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:200:

55

EP 0 592 106 B1

Gln Thr Ser Val Arg Pro Lys Lys Val Arg Phe Asp Pro Glu Lys Lys
1 5 10 15

5

(201) INFORMATION FOR SEQ ID NO:201

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:201:

Gln Thr Ser Val Arg Ser Gly Lys Val Arg Ser Glu Pro Glu Thr Lys
1 5 10 15

20

(202) INFORMATION FOR SEQ ID NO:202

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:202:

Val Thr Asn Leu Arg Pro Gly Lys Val Arg Ser Asp Ala Glu Lys Lys
1 5 10 15

35

(203) INFORMATION FOR SEQ ID NO:203

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:

50

Val Thr Asp Leu Arg Pro Gly Lys Val Arg Ser Asp Ala Glu Lys Lys
1 5 10 15

55

(204) INFORMATION FOR SEQ ID NO:204

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:204:

10 Gln Thr Ser Val Ser Pro Gly Asn Ile Arg Ser Glu Ser Asp Lys Lys
1 5 10 15

(205) INFORMATION FOR SEQ ID NO:205

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:205:

25

Lys Thr Ser Val Thr Pro Gly Lys Phe Arg Ser Glu Pro Glu Lys Lys
1 5 10 15

30

(206) INFORMATION FOR SEQ ID NO:206

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: peptide

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:206:

45 Val Thr Leu Leu Pro Pro Gly Arg Val Arg Ser Asp Ala Glu Lys Lys
1 5 10 15

(207) INFORMATION FOR SEQ ID NO:207

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

55

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:207:

Val Thr Leu Leu Pro Pro Gly Glu Val Arg Ser Asp Ala Glu Lys Lys
1 5 10 15

(208) INFORMATION FOR SEQ ID NO:208

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:

Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asp Ala Glu Arg Lys
1 5 10 15

(209) INFORMATION FOR SEQ ID NO:209

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:209:

Val Thr Leu Pro Pro Pro Gly Glx Val Arg Ser Asx Ala Glx Asn Lys
1 5 10 15

(210) INFORMATION FOR SEQ ID NO:210

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:210:

Val Thr Leu Pro Pro Pro Gln Gln Val Arg Ser Asp Ala Glu Lys Lys
1 5 10 15

(211) INFORMATION FOR SEQ ID NO:211

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:211:

10 Val Thr Leu Pro Pro Gly Gln Val Thr Ser Asp Ala Glu Lys Lys
1 5 10 15

(212) INFORMATION FOR SEQ ID NO:212

15 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

(B) TYPE: amino acid

20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:212:

25 Val Thr Leu Pro Pro Ala Gly Gln Val Arg Ser Asp Ala Glu Lys Arg
1 5 10 15

30 (213) INFORMATION FOR SEQ ID NO:213

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 16 amino acids

35 (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:213:

45 Ala Leu Ser Pro Ser Ser Gly Gln Ser Ser Ser Ala Ser Glu Arg Leu
1 5 10 15

(214) INFORMATION FOR SEQ ID NO:214

50 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

55 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:214:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
 1 5 10 15

Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser
 20 25

(215) INFORMATION FOR SEQ ID NO:215

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Val
 1 5 10 15

Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser
 20 25

(216) INFORMATION FOR SEQ ID NO:216

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216:

Glu Lys Val Gly Gly Leu Gln Pro Gly Thr Gly Ala Pro Gly Lys Ala
 1 5 10 15

Ser Arg Gly Asp Ser Gln Arg Pro Glu Ser
 20 25

(217) INFORMATION FOR SEQ ID NO:217

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:217:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser
20 25

(218) INFORMATION FOR SEQ ID NO:218

(i) **SEQUENCE CHARACTERISTICS:**

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:218:

Glu Lys Met Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser
20 25

(219) INFORMATION FOR SEQ ID NO:219

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:219:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser
20 25

(220) INFORMATION FOR SEQ ID NO:220

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:220:

5

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

10

Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr
20 25

(221) INFORMATION FOR SEQ ID NO:221

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:221:

25

Glu Lys Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

30

Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr
20 25

(222) INFORMATION FOR SEQ ID NO:222

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:222:

45

Glu Asn Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

50

Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr
20 25

(223) INFORMATION FOR SEQ ID NO:223

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223:

Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr
20 25

(224) INFORMATION FOR SEQ ID NO:224

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:224:

Glu Lys Val Gly Gly Leu Gln Ser Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Thr Ser Gln Arg Ala Glu Ser
20 25

(225) INFORMATION FOR SEQ ID NO:225

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:225:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Gly Ile Ser Gln Arg Ala Glu Arg
20 25

(226) INFORMATION FOR SEQ ID NO:226

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:226:

10 **Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ser**
1 5 10 15

15 **Ala Lys Gly Asx Ser Glx Arg Ala Gln Ser**
20 25

(227) INFORMATION FOR SEQ ID NO:227

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:227:

30 **Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala**
1 5 10 15

35 **Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser**
20 25

(228) INFORMATION FOR SEQ ID NO:228

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:228:

50 **Glu Lys Val Gly Gly Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala**
1 5 10 15

55 **Ser Lys Gly Ser Ser Gln Arg Ala Glu Ser**
20 25

(229) INFORMATION FOR SEQ ID NO:229

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:229:

Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Arg Lys Ala
1 5 10 15
Ser Lys Gly Asn Ser Gln Arg Ala Glu Ser
20 25

(230) INFORMATION FOR SEQ ID NO:230

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:230:

Glu Lys Met Gly Asn Leu Gln Pro Gly Ser Gly Thr Pro Gly Lys Ala
1 5 10 15
Ser Lys Gly Asn Ser Gln Arg Pro Asp Ser
20 25

(231) INFORMATION FOR SEQ ID NO:231

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:231:

Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15
Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr
20 25

EP 0 592 106 B1

(232) INFORMATION FOR SEQ ID NO:232

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:232:

15 **Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp**
1 5 10 15

Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr
20 25

20

(233) INFORMATION FOR SEQ ID NO:233

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:233:

35 **Glu Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Arg Asp**
1 5 10 15

Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr
20 25

40

(234) INFORMATION FOR SEQ ID NO:234

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

55

Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr
20 25

(235) INFORMATION FOR SEQ ID NO:235

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:235:

Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(236) INFORMATION FOR SEQ ID NO:236

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:236:

Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Asp Lys Asp
1 5 10 15

Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(237) INFORMATION FOR SEQ ID NO:237

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:237:

Glu Lys Val Gly Gly Leu Thr Pro Gly Lys Gly Thr Pro Glu Lys Asp
5 1 5 10 15

Ser Lys Gly Asn Gly Arg Arg Ser Glu Thr
20 25

10

(238) INFORMATION FOR SEQ ID NO:238

(i) **SEQUENCE CHARACTERISTICS:**

15 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:238:

²⁵

Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
 1 5 10 15

Ser Lys Gly Asn Asp Arg Arg Ser Glu Thr
20 25

30

(239) INFORMATION FOR SEQ ID NO:239

(i) **SEQUENCE CHARACTERISTICS:**

35 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:239:

Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
45 1 5 10 15

Ser Lys Gly Asn Asp Lys Arg Ser Glu Thr
20 25

50

(240) INFORMATION FOR SEQ ID NO:240

(i) **SEQUENCE CHARACTERISTICS:**

55 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:240:

5

Glu Met Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

10

Ser Lys Gly Asn Ala Lys Arg Ser Glu Thr
20 25

(241) INFORMATION FOR SEQ ID NO:241

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:241:

25

Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

30

Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(242) INFORMATION FOR SEQ ID NO:242

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:242:

45

Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

50

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(243) INFORMATION FOR SEQ ID NO:243

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:243:

Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp
1 5 10 15

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(244) INFORMATION FOR SEQ ID NO:244

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:244:

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(245) INFORMATION FOR SEQ ID NO:245

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:245:

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(246) INFORMATION FOR SEQ ID NO:246

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:246:

10 **Glu Lys Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Glu Lys Asp**
1 5 10 15

15 **Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr**
20 25

(247) INFORMATION FOR SEQ ID NO:247

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:247:

30 **Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Asp**
1 5 10 15

35 **Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr**
20 25

(248) INFORMATION FOR SEQ ID NO:248

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:248:

50 **Asp Lys Met Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp**
1 5 10 15

55 **Ser Lys Gly Asn Ala Lys Gln Ser Glu Thr**
20 25

(249) INFORMATION FOR SEQ ID NO:249

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:249:

Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Asp Lys Asp
1 5 10 15
Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(250) INFORMATION FOR SEQ ID NO:250

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:250:

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15
Ser Lys Gly Asn Ala Glu Lys Ser Glu Thr
20 25

(251) INFORMATION FOR SEQ ID NO:251

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:251:

Glu Gln Val Gly Asp Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15
Thr Lys Gly Asn Ala Arg Arg Ser Glu Thr
20 25

EP 0 592 106 B1

(252) INFORMATION FOR SEQ ID NO:252

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:252:

15 **Glu Asn Val Gly Asp Leu Lys Pro Gly Lys Gly Ala Pro Glu Lys Asp**
1 5 10 15
Ser Lys Gly Asn Ala Arg Arg Ser Glu Thr
20 25

20

(253) INFORMATION FOR SEQ ID NO:253

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:253:

35 **Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Asp Lys Asp**
1 5 10 15
Ser Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

40

(254) INFORMATION FOR SEQ ID NO:254

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:254:

55

EP 0 592 106 B1

Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

5 Ser Lys Gly Asn Ala Lys Lys Ser Gly Thr
20 25

(255) INFORMATION FOR SEQ ID NO:255

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

15

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:255:

20

Asp Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

25

Thr Lys Gly Asn Pro Lys Arg Ser Glu Thr
20 25

(256) INFORMATION FOR SEQ ID NO:256

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

35

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:256:

40

Asp Gln Val Gly Gly Leu Gln Pro Gly Gln Gly Thr Pro Glu Lys Asn
1 5 10 15

45

Thr Lys Gly Asn Pro Lys Arg Ser Asp Thr
20 25

(257) INFORMATION FOR SEQ ID NO:257

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

55

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:257:

Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Glu Lys Asp
1 5 10 15

Ile Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(258) INFORMATION FOR SEQ ID NO:258

(i) **SEQUENCE CHARACTERISTICS:**

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:258:

Asp Lys Val Gly Gly Leu Lys Pro Gly Lys Arg Thr Pro Glu Lys Asp
1 5 10 15

Asn Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(259) INFORMATION FOR SEQ ID NO:259

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:259:

Asp Lys Val Gly Gly Leu Lys Leu Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

Thr Lys Gly Asn Ala Lys Lys Ser Glu Thr
20 25

(260) INFORMATION FOR SEQ ID NO:260

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:260:

5 Glu Lys Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp
 1 5 10 15

10 Ser Lys Gly Asn Ala Asn Thr Ser Glu Thr
 20 25

(261) INFORMATION FOR SEQ ID NO:261

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:261:

25 Glu His Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
 1 5 10 15

30 Ser Lys Gly Asn Ala Gly Arg Ser Glu Thr
 20 25

(262) INFORMATION FOR SEQ ID NO:262

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:262:

45 Glu Gln Val Gly Gly Leu Gln Pro Gly Asn Gly Thr Pro Glu Lys Asp
 1 5 10 15

50 Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr
 20 25

(263) INFORMATION FOR SEQ ID NO:263

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:263:

Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu
1 5 10 15

Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr
20 25

(264) INFORMATION FOR SEQ ID NO:264

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:264:

Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Glu
1 5 10 15

Ser Lys Gly Asp Ser Lys Arg Pro Glu Thr
20 25

(265) INFORMATION FOR SEQ ID NO:265

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:265:

Glu Lys Glu Gly Gly Leu Gln Pro Gly Lys Gly Ser Pro Glu Lys Glu
1 5 10 15

Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr
20 25

(266) INFORMATION FOR SEQ ID NO:266

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:266:

10 **Glu Lys Asp Gly Gly Leu Gln Pro Gly Lys Gly Thr Pro Glu Lys Asp**
1 5 10 15

15 **Ser Lys Gly Asp Ser Lys Arg Val Glu Met**
20 25

(267) INFORMATION FOR SEQ ID NO:267

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:267:

30 **Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp**
1 5 10 15

35 **Thr Thr Gly Asp Ala Gln Arg Ser Glu Thr**
20 25

(268) INFORMATION FOR SEQ ID NO:268

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:268:

50 **Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Glu Lys Asp**
1 5 10 15

55 **Thr Thr Gly Asn Ala Lys Gly Ser Glu Thr**
20 25

(269) INFORMATION FOR SEQ ID NO:269

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:269:

Glu Lys Val Gly Gly Ser Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15
Ser Lys Gly Asn Ala Lys Thr Ser Glu Thr
20 25

(270) INFORMATION FOR SEQ ID NO:270

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:270:

Ser Asp Gln Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Glu Lys Asp
1 5 10 15
Thr Lys Gly Asn Ala Arg Arg Ser Glu Ser
20 25

(271) INFORMATION FOR SEQ ID NO:271

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:271:

Glu Lys Ile Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro
1 5 10 15
Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr
20 25

EP 0 592 106 B1

(272) INFORMATION FOR SEQ ID NO:272

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:272:

15 **Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro**
1 5 10 15
Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr
20 25

(273) INFORMATION FOR SEQ ID NO:273

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:273:

35 **Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Pro**
1 5 10 15
Phe Lys Asp Asn Ala Lys Arg Ser Glu Thr
20 25

40

(274) INFORMATION FOR SEQ ID NO:274

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:274:

55

Glu Lys Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Leu
 1 5 10 15

Met Lys Glu Asn Ala Lys Arg Ser Glu Thr
 20 25

(275) INFORMATION FOR SEQ ID NO:275

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:275:

Glu Asn Leu Gly Gly Leu Gln Pro Gly Lys Gly Asp Pro Gly Lys Leu
 1 5 10 15

Lys Xaa Glu Asn Ala Lys Arg Pro Glu Thr
 20 25

(276) INFORMATION FOR SEQ ID NO:276

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:276:

Glu Lys Leu Gly Gly Leu Gln Pro Gly Asn Gly Asp Leu Gly Lys Pro
 1 5 10 15

Ser Lys Asp Asn Ala Lys Arg Ser Glu Thr
 20 25

(277) INFORMATION FOR SEQ ID NO:277

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:277:

Glu Lys Leu Gly Pro Leu Gln Leu Gly Lys Gly Asp Pro Gly Lys Pro
1 5 10 15

Ser Lys Asp Asp Ala Lys Arg Ser Glu Thr
20 25

(278) INFORMATION FOR SEQ ID NO:278

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:278:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Pro
1 5 10 15

Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr
20 25

(279) INFORMATION FOR SEQ ID NO:279

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:279:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Gly Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys Asp Asn Asp Lys Arg Ser Glu Thr
20 25

(280) INFORMATION FOR SEQ ID NO:280

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:280:

5

Glu Gln Val Gly Gly Leu Lys Ala Arg Lys Gly Thr Pro Glu Lys Asp
1 5 10 15

10

Thr Thr Gly Asn Ala Lys Arg Ser Glu Thr
20 25

(281) INFORMATION FOR SEQ ID NO:281

15

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:281:

25

Glu Met Val Gly Val Leu Glu Pro Gly Lys Gly Thr Pro Glu Lys Arg
1 5 10 15

30

Gln Glu Gly Asn Ala Lys Arg Ser Glu Thr
20 25

(282) INFORMATION FOR SEQ ID NO:282

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:282:

45

Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp
1 5 10 15

50

Ser Lys Asp Asp Ser Gln Lys Thr Glu Thr
20 25

(283) INFORMATION FOR SEQ ID NO:283

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:283:

Glu Gln Val Gly Gly Leu Gln Pro Lys Lys Gly Ser Pro Gly Lys Asp
1 5 10 15

10

Ser Lys Asp Asp Ser Gln Lys Thr Glu Arg
20 25

15 (284) INFORMATION FOR SEQ ID NO:284

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

20

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:284:

Gln Gln Val Pro Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Glu
1 5 10 15

30

Asp Lys Gly Thr Ser Ala Arg Asn Asp Thr
20 25

35 (285) INFORMATION FOR SEQ ID NO:285

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

40

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:285:

Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp
1 5 10 15

50

Asp Lys Gly Thr Ser Ala Lys Asn Glu Thr
20 25

55 (286) INFORMATION FOR SEQ ID NO:286

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:286:

10 Gln Gln Val Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Asp
1 5 10 15
Asp Lys Gly Thr Ser Ala Lys Asn Glu Met
20 25
15

(287) INFORMATION FOR SEQ ID NO:287

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:287:

30 Gln Gln Lys Pro Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Thr Ser Ser Thr Ser Glu Thr
20 25
35

(288) INFORMATION FOR SEQ ID NO:288

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:288:

50 Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25
55

(289) INFORMATION FOR SEQ ID NO:289

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:289:

Glu Gln Gln Pro Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(290) INFORMATION FOR SEQ ID NO:290

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:290:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser
20 25

(291) INFORMATION FOR SEQ ID NO:291

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:291:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Lys Gln
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

EP 0 592 106 B1

(292) INFORMATION FOR SEQ ID NO:292

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:292:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(293) INFORMATION FOR SEQ ID NO:293

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:293:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(294) INFORMATION FOR SEQ ID NO:294

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:294:

EP 0 592 106 B1

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser
20 25

(295) INFORMATION FOR SEQ ID NO:295

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:295:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Phe Glu Ser
20 25

(296) INFORMATION FOR SEQ ID NO:296

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:296:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln
1 5 10 15

Lys Gln Gly Lys Ser Ser Thr Phe Glu Ser
20 25

(297) INFORMATION FOR SEQ ID NO:297

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:297:

Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(298) INFORMATION FOR SEQ ID NO:298

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:298:

25 Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln
 1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(299) INFORMATION FOR SEQ ID NO:299

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:299:

45 Glu Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Gln
 1 5 10 15

Lys Lys Ser Asn Ser Ser Thr Ser Glu Ser
20 25

(300) INFORMATION FOR SEQ ID NO:300

(i) SEQUENCE CHARACTERISTICS:

55 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:300:

5

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Glu
1 5 10 15

10

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(301) INFORMATION FOR SEQ ID NO:301

15

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:301:

25

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Glu
1 5 10 15

30

Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser
20 25

(302) INFORMATION FOR SEQ ID NO:302

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:302:

45

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Val Pro Gly Gln Glu
1 5 10 15

50

Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser
20 25

(303) INFORMATION FOR SEQ ID NO:303

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:303:

Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(304) INFORMATION FOR SEQ ID NO:304

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:304:

Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly
1 5 10 15
Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(305) INFORMATION FOR SEQ ID NO:305

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:305:

Glu Gln Gln Pro Glu Ala Lys Pro Gly Lys Gly Thr His Gly Lys Gln
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser
20 25

(306) INFORMATION FOR SEQ ID NO:306

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:306:

10 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr His Gly Lys Glu
1 5 10 15

15 Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser
20 25

(307) INFORMATION FOR SEQ ID NO:307

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:307:

30 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Gly Gln Gly
1 5 10 15

35 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(308) INFORMATION FOR SEQ ID NO:308

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:308:

50 Gln Gln Gln Ala Glu Leu Lys Pro Gly Arg Gly Thr Pro Gly Gln Glu
1 5 10 15

55 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(309) INFORMATION FOR SEQ ID NO:309

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:309:

Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(310) INFORMATION FOR SEQ ID NO:310

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:310:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
20 25

(311) INFORMATION FOR SEQ ID NO:311

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:311:

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15
Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
20 25

EP 0 592 106 B1

(312) INFORMATION FOR SEQ ID NO:312

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:312:

15 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15
Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
20 25

20

(313) INFORMATION FOR SEQ ID NO:313

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:313:

35 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15
Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser
20 25

40

(314) INFORMATION FOR SEQ ID NO:314

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:314:

55

Gln Gln Gln Ala Glu Val Arg Pro Gly Lys Gly Thr Pro Gly His Glu
 1 5 10 15

Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
 20 25

(315) INFORMATION FOR SEQ ID NO:315

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:315:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu
 1 5 10 15

Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser
 20 25

(316) INFORMATION FOR SEQ ID NO:316

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:316:

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln
 1 5 10 15

Lys Lys Gly Lys Ser Ser Ala Ser Glu Ser
 20 25

(317) INFORMATION FOR SEQ ID NO:317

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:317:

His Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(318) INFORMATION FOR SEQ ID NO:318

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:318:

Glu Gln Gln Val Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(319) INFORMATION FOR SEQ ID NO:319

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:319:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Gln Gly Thr Ser Ser Thr Ser Glu Ser
20 25

(320) INFORMATION FOR SEQ ID NO:320

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:320:

5

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly His Asp
1 5 10 15

10

Asn Lys Gly Thr Ser Ser Thr Ser Glu Ser
20 25

(321) INFORMATION FOR SEQ ID NO:321

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

20

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:321:

25

Gln Gln Gln Ala Glu Val Arg Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15

30

Lys Lys Gly Arg Ser Ser Thr Ser Glu Ser
20 25

(322) INFORMATION FOR SEQ ID NO:322

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

40

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:322:

45

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

50

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(323) INFORMATION FOR SEQ ID NO:323

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:323:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(324) INFORMATION FOR SEQ ID NO:324

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:324:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Asp Ser
20 25

(325) INFORMATION FOR SEQ ID NO:325

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:325:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Ser Pro Gly Gln Gln
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(326) INFORMATION FOR SEQ ID NO:326

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:326:

Gln His Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Lys Lys Asn Lys Ser Ser Thr Ser Glu Ser
20 25

(327) INFORMATION FOR SEQ ID NO:327

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:327:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Asn Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(328) INFORMATION FOR SEQ ID NO:328

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:328:

Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Ile Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(329) INFORMATION FOR SEQ ID NO:329

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:329:

15 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser
20 25

20

(330) INFORMATION FOR SEQ ID NO:330

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:330:

35 Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser
40 20 25

40

(331) INFORMATION FOR SEQ ID NO:331

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:331:

55

Gln Gln Gln Thr Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
 1 5 10 15

Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser
 20 25

(332) INFORMATION FOR SEQ ID NO:332

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:332:

Glu Gln Gln Ala Glu Leu Arg Thr Gly Lys Gly Thr Pro Gly Gln Glu
 1 5 10 15

Arg Lys Gly Lys Ser Ser Thr Ser Glu Ser
 20 25

(333) INFORMATION FOR SEQ ID NO:333

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:333:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
 1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Phe Glu Ser
 20 25

(334) INFORMATION FOR SEQ ID NO:334

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:334:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Thr Gly Ala Pro Gly Gln Glu
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(335) INFORMATION FOR SEQ ID NO:335

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:335:

Gln Gln Gln Pro Glu Val Arg Pro Gly Lys Gly Thr His Ala Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(336) INFORMATION FOR SEQ ID NO:336

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:336:

Gln Gln Gln Pro Glu Val Arg Pro Gly Lys Asp Thr His Ala Lys Gln
1 5 10 15

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(337) INFORMATION FOR SEQ ID NO:337

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

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(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:337:

5

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Glu Gln Glu
1 5 10 15

10

Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(338) INFORMATION FOR SEQ ID NO:338

15

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:338:

25

Glu Gln Gln Thr Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

30

Lys Lys Gly Arg Ser Ser Thr Ser Glu Ala
20 25

(339) INFORMATION FOR SEQ ID NO:339

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:339:

45

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu
1 5 10 15

50

Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser
20 25

(340) INFORMATION FOR SEQ ID NO:340

55

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:340:

Gln Gln Gln Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu
 1 5 10 15
 Lys Lys Ser Lys Pro Ser Thr Ser Glu Ser
 20 25

(341) INFORMATION FOR SEQ ID NO:341

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:341:

Gln Gln Arg Ala Glu Leu Lys Pro Gly Lys Asp Thr Pro Gly Arg Glu
 1 5 10 15
 Lys Lys Asn Lys Pro Ser Thr Ser Glu Ser
 20 25

(342) INFORMATION FOR SEQ ID NO:342

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:342:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu
 1 5 10 15
 Lys Lys Ser Thr Ser Ser Thr Ser Glu Ser
 20 25

(343) INFORMATION FOR SEQ ID NO:343

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:343:

10 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Lys Ser Thr Ser Ser Thr Ser Asp Ser
15 20 25

(344) INFORMATION FOR SEQ ID NO:344

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:344:

30 Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Ile Gln Gln
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
35 20 25

(345) INFORMATION FOR SEQ ID NO:345

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:345:

50 Gln Gln Gln Ala Glu Phe Lys Pro Gly Lys Gly Thr Pro Gly Arg Glu
1 5 10 15

His Arg Ser Lys Pro Ser Thr Ser Glu Ser
55 20 25

(346) INFORMATION FOR SEQ ID NO:346

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:346:

Gln Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Leu Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Asp Ser
20 25

(347) INFORMATION FOR SEQ ID NO:347

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:347:

Gln Gln Gln Pro Glu Val Lys Pro Gly Lys Gly Ala Pro Gly Lys Gly
1 5 10 15
Asn Thr Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(348) INFORMATION FOR SEQ ID NO:348

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:348:

Glu Gln Gln Ala Glu Val Arg Ala Gly Lys Gly Ser Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(349) INFORMATION FOR SEQ ID NO:349

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:349:

15 Gln Gln Leu Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15

Lys Lys Gly Ile Ser Ser Thr Ser Glu Ser
20 25

20

(350) INFORMATION FOR SEQ ID NO:350

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:350:

35 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Lys Pro Glu Gln Glu
1 5 10 15

Lys Lys Gly Thr Ser Ser Thr Ser Glu Ser
40 20 25

40

(351) INFORMATION FOR SEQ ID NO:351

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:351:

55

Gln Gln Gln Pro Glu Leu Lys Pro Gly Lys Gly Arg Asn Gly Lys Glu
1 5 10 15

Asn Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(352) INFORMATION FOR SEQ ID NO:352

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:352:

Gln Gln Gln Thr Glu Leu Arg Pro Gly Arg Gly Thr Thr Gly Gln Glu
1 5 10 15

Arg Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(353) INFORMATION FOR SEQ ID NO:353

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:353:

Gln His Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly His Glu
1 5 10 15

Asn Lys Val Thr Ser Ser Thr Ser Glu Ser
20 25

(354) INFORMATION FOR SEQ ID NO:354

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:354:

5 Gln Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
 1 5 10 15

 Gln Lys Ala Lys Ser Ser Thr Ser Glu Ser
 20 25

10 (355) INFORMATION FOR SEQ ID NO:355

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 26 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:355:

25 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
 1 5 10 15

 Lys Thr Gly Thr Ser Ser Thr Thr Glu Ser
 20 25

30 (356) INFORMATION FOR SEQ ID NO:356

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 26 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:356:

45 Gln Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Gly Gln Glu
 1 5 10 15

 Lys Lys Ser Thr Ser Ser Ala Ser Glu Ser
 20 25

50 (357) INFORMATION FOR SEQ ID NO:357

(i) SEQUENCE CHARACTERISTICS:

55 (A) LENGTH: 26 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:357:

5 Glu Gln Gln Thr Val Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Gln
 1 5 10 15
10 Lys Lys Gly Thr Ser Ala Thr Asn Glu Ser
 20 25

(358) INFORMATION FOR SEQ ID NO:358

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:358:

25 Gln Gln Leu Thr Glu Leu Lys Pro Gly Asn Gly Thr Pro Gly Gln Glu
 1 5 10 15
30 Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser
 20 25

(359) INFORMATION FOR SEQ ID NO:359

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:359:

45 Gln Gln Gln Ser Val Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
 1 5 10 15
50 Lys Lys Gly Thr Ser Ser Thr Ser Lys Ser
 20 25

(360) INFORMATION FOR SEQ ID NO:360

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:360:

Leu Gln Gln Pro Val Leu Lys Pro Gly Lys Gly Ser His Gly Lys Gln
1 5 10 15

Lys Lys Asp Lys Ser Ser Thr Ser Glu Ser
20 25

(361) INFORMATION FOR SEQ ID NO:361

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:361:

Glu Gln Gln Pro Glu Thr Lys Pro Gly Lys Gly Thr Leu Gly Lys Gln
1 5 10 15

Lys Lys Ser Lys Ser Ser Thr Ser Glu Ser
20 25

(362) INFORMATION FOR SEQ ID NO:362

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:362:

Gln Gln Gln Ala Glu Leu Lys Pro Gly Gln Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Lys Asn Lys Ser Ser Thr Pro Glu Phe
20 25

(363) INFORMATION FOR SEQ ID NO:363

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:363:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15
Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr
20 25

(364) INFORMATION FOR SEQ ID NO:364

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:364:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15
Lys Gln Gly Thr Ser Thr Thr Ser Glu Thr
20 25

(365) INFORMATION FOR SEQ ID NO:365

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:365:

Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15
Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr
20 25

EP 0 592 106 B1

(366) INFORMATION FOR SEQ ID NO:366

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:366:

15 Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15

Lys Gln Asp Thr Ser Ser Thr Ser Glu Thr
20 25

20

(367) INFORMATION FOR SEQ ID NO:367

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:367:

35 Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15

Lys Gln Gly Thr Ser Ser Thr Ser Gly Thr
20 25

40

(368) INFORMATION FOR SEQ ID NO:368

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:368:

55

Glu Gln Gln Ala Glu Val Lys Pro Gly Lys Gly Asn Pro Glu Gln Pro
 1 5 10 15

Lys Gln Gly Thr Ser Ser Thr Ser Glu Thr
 20 25

(369) INFORMATION FOR SEQ ID NO:369

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:369:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro
 1 5 10 15

Lys Gln Val Thr Ser Ser Thr Ser Glu Thr
 20 25

(370) INFORMATION FOR SEQ ID NO:370

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:370:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Pro Glu Gln Pro
 1 5 10 15

Lys Gln Ile Thr Ser Ser Thr Ser Glu Thr
 20 25

(371) INFORMATION FOR SEQ ID NO:371

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:371:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Arg Gly Asn Pro Glu Gln Pro
1 5 10 15

Lys Gln Val Thr Ser Ser Thr Ser Glu Thr
20 25

(372) INFORMATION FOR SEQ ID NO:372

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:372:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Arg Gly Asn Pro Glu Gln Pro
1 5 10 15

Lys His Val Thr Ser Ser Thr Ser Glu Thr
20 25

(373) INFORMATION FOR SEQ ID NO:373

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:373:

Glu Gln Gln Ala Glu Leu Arg Pro Gly Lys Gly Asn Thr Glu Gln Pro
1 5 10 15

Lys Gln Val Thr Ser Ser Thr Ser Glu Thr
20 25

(374) INFORMATION FOR SEQ ID NO:374

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:374:

5 Glu Gln Gln Ala Glu Leu Lys Pro Gly Lys Gly Asn Thr Glu Gln Pro
 1 5 10 15
10 Lys Leu Ile Thr Ser Ser Thr Ser Glu Thr
 20 25

(375) INFORMATION FOR SEQ ID NO:375

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:375:

25 Thr Gly Gln Ala Glu Leu Arg Pro Gly Lys Gly Ala Pro Glu Gln Gly
 1 5 10 15
30 Lys Lys Gly Lys Ser Ser Thr Ser Asp Arg
 20 25

(376) INFORMATION FOR SEQ ID NO:376

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:376:

45 Gln Tyr Gln Ala Glu Leu Arg Pro Gly Lys Gly Thr Pro Arg Gln Gln
 1 5 10 15
50 Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
 20 25

(377) INFORMATION FOR SEQ ID NO:377

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:377:

Gln Gln Gln Ala Val Leu Arg His Gly Lys Gly Thr His Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Thr Ser Glu Ser
20 25

(378) INFORMATION FOR SEQ ID NO:378

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:378:

Gln Gln Gln Thr Lys Leu Gly Pro Gly Arg Gly Thr Pro Gly Gln Gly
1 5 10 15
Arg Lys Gly Lys Ser Ser Thr Ser Gly Ser
20 25

(379) INFORMATION FOR SEQ ID NO:379

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:379:

Glu Gln Gln Ala Glu Leu Arg Ala Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15
Lys Lys Gly Lys Ser Ser Val Tyr Phe Ala
20 25

(380) INFORMATION FOR SEQ ID NO:380

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:380:

10 Glu Gln Gln Ala Glu Leu Lys Ala Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

15 Lys Gln Gly Glu Ser Thr Arg Ser Glu Thr
20 25

(381) INFORMATION FOR SEQ ID NO:381

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:381:

30 Gln Gln Lys Ala Glu Leu Ala Ala Ser Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

35 Lys Lys Gly Arg Ser Ser Thr Ser Glu Ser
20 25

(382) INFORMATION FOR SEQ ID NO:382

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:382:

50 Gln Gln Gln Thr Glu Leu Arg Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

55 Lys Arg Gly Lys Ser Ser Asn Leu Arg Leu
20 25

(383) INFORMATION FOR SEQ ID NO:383

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:383:

Glu Lys Val Gly Gly Leu Gln Gly Ser Ser Phe Asp Pro Gly Lys Ala
1 5 10 15
Ser Lys Gly Thr Ser Gln Arg Ala Glu Thr
20 25

(384) INFORMATION FOR SEQ ID NO:384

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:384:

Glu Gln Gln Ala Asp Leu Lys Leu Gly Lys Gly Asn Pro Glu Gln Pro
1 5 10 15
Lys Leu Ala Thr Pro Ser Thr Ser Glu Thr
20 25

(385) INFORMATION FOR SEQ ID NO:385

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:385:

Glu Gln Val Gly Gly Leu Lys Pro Gly Lys Gly Thr Pro Asp Lys Ser
1 5 10 15
Asp Val Lys Asp Asn Ala Lys Ser Glu Thr
20 25

EP 0 592 106 B1

(386) INFORMATION FOR SEQ ID NO:386

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:386:

15 Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly His Pro
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

20

(387) INFORMATION FOR SEQ ID NO:387

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:387:

35 Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

40

(388) INFORMATION FOR SEQ ID NO:388

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:388:

55

Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

5 Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr
20 25

(389) INFORMATION FOR SEQ ID NO:389

10

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
15 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:389:

20

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

25

Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

(390) INFORMATION FOR SEQ ID NO:390

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
35 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:390:

40

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

45

Ser Lys Asn Thr Ser Lys Thr Thr Glu Thr
20 25

(391) INFORMATION FOR SEQ ID NO:391

50

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
55 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:391:

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asp Pro
1 5 10 15

Ser Lys Thr Thr Ser Lys Thr Thr Glu Thr
20 25

(392) INFORMATION FOR SEQ ID NO:392

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:392:

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

Ser Lys Thr Thr Ser Lys Thr Thr Glu Thr
20 25

(393) INFORMATION FOR SEQ ID NO:393

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:393:

Asp His Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

Ser Lys Asn Thr Ser Lys Thr Thr Glu Thr
20 25

(394) INFORMATION FOR SEQ ID NO:394

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:394:

5

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

10

Ser Arg Ser Thr Ser Lys Thr Thr Glu Thr
20 25

(395) INFORMATION FOR SEQ ID NO:395

15

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:395:

25

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ala Gly Ser Pro Gly Asn Pro
1 5 10 15

30

Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr
20 25

(396) INFORMATION FOR SEQ ID NO:396

35

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:396:

45

Glu Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

50

Ser Lys Ser Thr Ser Lys Thr Ser Glu Thr
20 25

(397) INFORMATION FOR SEQ ID NO:397

55

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:397:

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

10

Ser Lys Asn Thr Ser Lys Thr Ile Glu Thr
20 25

15

(398) INFORMATION FOR SEQ ID NO:398

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:398:

Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asp Pro
1 5 10 15

30

Ser Lys Asn Thr Ser Lys Thr Pro Glu Thr
20 25

35

(399) INFORMATION FOR SEQ ID NO:399

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:399:

Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

50

Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

55

(400) INFORMATION FOR SEQ ID NO:400

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:400:

10 Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Asn Thr Ser Glu Thr Thr Glu Thr
20 25
15

(401) INFORMATION FOR SEQ ID NO:401

(i) SEQUENCE CHARACTERISTICS:

20

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:401:

30 Asp Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Asn Thr Ser Glu Thr Thr Glx Thr
20 25
35

(402) INFORMATION FOR SEQ ID NO:402

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:402:

50

Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Ser Glu Thr
20 25
55

(403) INFORMATION FOR SEQ ID NO:403

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:403:

Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Ser Thr Ser Arg Thr Thr Glu Thr
20 25

(404) INFORMATION FOR SEQ ID NO:404

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:404:

Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Ala Glu Thr
20 25

(405) INFORMATION FOR SEQ ID NO:405

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:405:

Asp Gln Gln Pro Asp Leu Lys Pro Ser Ser Gly Phe Pro Gly Asn Pro
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

EP 0 592 106 B1

(406) INFORMATION FOR SEQ ID NO:406

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:406:

15 Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Lys Pro
1 5 10 15

Ser Lys Ser Thr Ser Lys Thr Asn Glu Thr
20 25

20

(407) INFORMATION FOR SEQ ID NO:407

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:407:

35 Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

Ser Lys Ser Thr Phe Lys Thr Ser Glu Thr
20 25

40

(408) INFORMATION FOR SEQ ID NO:408

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:408:

55

EP 0 592 106 B1

Glu Gln Gln Pro Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

Ser Lys Ser Thr Ser Thr Thr Ser Glu Thr
20 25

(409) INFORMATION FOR SEQ ID NO:409

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:409:

Glu Gln Gln Leu Ser Leu Lys Pro Ser Ser Gly Ser Pro Gly Asn Pro
1 5 10 15

Ser Lys Ser Thr Ser Lys Thr Thr Glu Thr
20 25

(410) INFORMATION FOR SEQ ID NO:410

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:410:

Gln Gln Gln Pro Gly Leu Lys Pro Ser Phe Gly Pro Pro Gly Lys Pro
1 5 10 15

Ser Gln Ser Thr Ser Lys Thr Thr Glu Thr
20 25

(411) INFORMATION FOR SEQ ID NO:411

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:411:

Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
5 1 5 10 15

Thr Lys Ser Asn Ser Lys Gln Thr Asp Thr
20 25

10

(412) INFORMATION FOR SEQ ID NO:412

(i) **SEQUENCE CHARACTERISTICS:**

15 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:412:

25 Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
 1 5 10 15

Ala Lys Ser Asn Ser Lys Gln Thr Asp Thr
20 25

30

(413) INFORMATION FOR SEQ ID NO:413

(i) **SEQUENCE CHARACTERISTICS:**

35 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:413:

Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
1 5 10 15

Ala Met Ser Asn Ser Lys Gln Thr Asp Thr
20 25

50

(414) INFORMATION FOR SEQ ID NO:414

(i) SEQUENCE CHARACTERISTICS:

55 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:414:

5
Gln Gln Lys Pro Gly Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
1 5 10 15
10
Ala Ile Ser Asn Ser Lys Gln Thr Asp Thr
20 25

(415) INFORMATION FOR SEQ ID NO:415

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:415:

25
Gln Gln Lys Pro Gly Leu Gln Pro Ser Ser Gly Ser Pro Gly Lys Ala
1 5 10 15
30
Ala Ile Ser Asn Ser Lys Gln Ser Asn Thr
20 25

(416) INFORMATION FOR SEQ ID NO:416

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:416:

45
Gln Gln Lys Pro Gly Leu Gln Pro Ser Ser Gly Ser Pro Gly Lys Ala
1 5 10 15
50
Ala Ile Ser Asn Ser Lys Gln Ala Asn Thr
20 25

(417) INFORMATION FOR SEQ ID NO:417

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids

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(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:417:

Gln Gln Lys Pro Val Leu Ala Pro Ser Ser Gly Ser Pro Gly Lys Ser
1 5 10 15

Ala Met Ser Asn Ser Lys Gln Ile Asp Thr
20 25

(418) INFORMATION FOR SEQ ID NO:418

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:418:

Gln Gln Lys Pro Ser Leu Gln Pro Ser Ser Asp Ser Pro Gly Lys Ala
1 5 10 15

Ala Met Ser Asn Ser Lys Gln Ala Asp Thr
20 25

(419) INFORMATION FOR SEQ ID NO:419

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:419:

Glu Arg Val Gly Asp Leu Glu Pro Gly Arg Gly Ile Pro Gly Lys Ala
1 5 10 15

Pro Lys Gly Asp Ser Lys Lys Ile Glu Thr
20 25

(420) INFORMATION FOR SEQ ID NO:420

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:420:

10 Glu Arg Val Gly Asp Leu Glu Pro Glu Arg Gly Ile Pro Gly Lys Ala
1 5 10 15

15 Pro Lys Gly Asp Ser Lys Lys Ile Glu Thr
20 25

(421) INFORMATION FOR SEQ ID NO:421

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:421:

30 Glu Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

35 Pro Lys Gly Asp Ser Lys Lys Thr Glu Thr
20 25

(422) INFORMATION FOR SEQ ID NO:422

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:422:

50 Glu Gln Val Gly Gly Leu Gln Pro Gly Lys Gly Thr Ser Gly Lys Ala
1 5 10 15

55 Ser Lys Gly Asp Ser Lys Lys Thr Glu Thr
20 25

(423) INFORMATION FOR SEQ ID NO:423

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:423:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asx
1 5 10 15
Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr
20 25

(424) INFORMATION FOR SEQ ID NO:424

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:424:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15
Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr
20 25

(425) INFORMATION FOR SEQ ID NO:425

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:425:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15
Ser Arg Gly Asn Ser Lys Arg Ala Glu Thr
20 25

EP 0 592 106 B1

(426) INFORMATION FOR SEQ ID NO:426

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:426:

15 **Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp**
1 5 10 15
Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr
20 25

20

(427) INFORMATION FOR SEQ ID NO:427

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:427:

35 **Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp**
1 5 10 15
Ser Lys Gly Asn Ala Lys Arg Ala Glu Thr
20 25

40

(428) INFORMATION FOR SEQ ID NO:428

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:428:

55

Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asp Ser Arg Arg Ala Glu Thr
20 25

(429) INFORMATION FOR SEQ ID NO:429

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:429:

Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ser Arg Arg Ala Glu Thr
20 25

(430) INFORMATION FOR SEQ ID NO:430

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:430:

Gln Gln Val Gly Gly Leu Glu Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asx Ser Lys Arg Ala Glu Thr
20 25

(431) INFORMATION FOR SEQ ID NO:431

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:431:

Glu Gln Leu Gly Asp Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Ala
1 5 10 15

Ser Lys⁻Gly⁻ Asn Ser Lys Arg Ala Glu Thr
20 25

(432) INFORMATION FOR SEQ ID NO:432

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:432:

Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Thr Gly Lys Asp
1 5 10 15

Ser Lys Gly Asp Ser Lys Arg Ala Glu Thr
20 25

(433) INFORMATION FOR SEQ ID NO:433

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:433:

Gln Gln Val Gly Gly Val Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr
20 25

(434) INFORMATION FOR SEQ ID NO:434

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:434:

5 Gln Gln Val Gly Gly Val Gln Pro Gly Arg Gly Ile Pro Gly Lys Asp
 1 5 10 15
10 Ser Lys Gly Asn Ser Lys Arg Pro Glu Thr
 20 25

(435) INFORMATION FOR SEQ ID NO:435

15 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 26 amino acids

 (B) TYPE: amino acid

 (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:435:

25 Glu Gln Val Gly Gly Val Gln Pro Gly Arg Gly Ile Pro Gly Lys Asp
 1 5 10 15
30 Ser Lys Gly Asp Ser Lys Arg Pro Glu Thr
 20 25

(436) INFORMATION FOR SEQ ID NO:436

35 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 26 amino acids

 (B) TYPE: amino acid

 (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:436:

45 Gln Gln Val Gly Gly Val Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
 1 5 10 15
50 Ser Asn Gly Asp Ser Lys Arg Pro Glu Thr
 20 25

(437) INFORMATION FOR SEQ ID NO:437

55 (i) SEQUENCE CHARACTERISTICS:

 (A) LENGTH: 26 amino acids

 (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:437:

Gln Lys Val Gly Gly Val Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ser Lys Arg Thr Glu Thr
20 25

(438) INFORMATION FOR SEQ ID NO:438

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:438:

Gln Glu Val Gly Gly Val Glx Pro Gly Arg Gly Thr Pro Gly Lys Asx
1 5 10 15

Ser Lys Gly Asx Ser Lys Arg Ala Glu Thr
20 25

(439) INFORMATION FOR SEQ ID NO:439

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:439:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Asn Gly Asp Ser Lys Gln Ala Glx Thr
20 25

EP 0 592 106 B1

(440) INFORMATION FOR SEQ ID NO:440

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:440:

15 **Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Ser Pro Gly Lys Asp**
1 5 10 15

Thr Asn Gly Asp Ser Lys Glu Ala Glx Thr
20 25

20

(441) INFORMATION FOR SEQ ID NO:441

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:441:

35 **Ala Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp**
1 5 10 15

Ser Asn Gly Asp Ser Lys Gln Ala Glx Ser
20 25

40

(442) INFORMATION FOR SEQ ID NO:442

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:442:

55

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Val
1 5 10 15

Ser Gln Gly Asp Ser Lys Gln Ala Glx Thr
20 25

(443) INFORMATION FOR SEQ ID NO:443

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:443:

Glu Gln Val Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Val
1 5 10 15

Ser Gln Gly Asp Ser Lys Glu Pro Glx Thr
20 25

(444) INFORMATION FOR SEQ ID NO:444

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:444:

Glu Gln Leu Gly Gly Leu Gln Pro Glu Arg Gly Thr Pro Gly Lys Glu
1 5 10 15

Ser Lys Gly Asn Ser Met Arg Ala Glu Thr
20 25

(445) INFORMATION FOR SEQ ID NO:445

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:445:

Glu Gln Val Gly Asp Leu Gln Pro Gly Arg Gly Asx Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ala Lys Arg Val Glu Thr
20 25

(446) INFORMATION FOR SEQ ID NO:446

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:446:

Glu Gln Val Gly Asp Leu Gln Pro Gly Arg Gly Asn Pro Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ala Gln Arg Pro Glu Thr
20 25

(447) INFORMATION FOR SEQ ID NO:447

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:447:

Gln Gln Val Gly Gly Val Gln Pro Gly Arg Gly Thr Leu Gly Lys Asp
1 5 10 15

Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr
20 25

(448) INFORMATION FOR SEQ ID NO:448

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:448:

5 Gln Glx Val Gly Gly Ala Glx Pro Gly Arg Gly Ser Pro Gly Lys Ala
 1 5 10 15
10 Ser Lys Gly Asx Ser Lys Arg Ala Glu Thr
 20 25

(449) INFORMATION FOR SEQ ID NO:449

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:449:

25 Gln Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Ser Pro Gly Lys Asp
 1 5 10 15
30 Ser Lys Gly Asn Ala Gln Arg Thr Glx Thr
 20 25

(450) INFORMATION FOR SEQ ID NO:450

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:450:

45 Asp Gln Val Gly Gly Leu Lys Pro Gly Arg Gly Thr Pro Gly Lys Asn
 1 5 10 15
50 Ser Asn Gly Asp Ser Lys Thr Pro Glx Thr
 20 25

(451) INFORMATION FOR SEQ ID NO:451

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid

EP 0 592 106 B1

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:451:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Ser Arg Glu Asp
1 5 10 15

Ser Lys Gly Asn Ser Lys Arg Ala Glu Thr
20 25

(452) INFORMATION FOR SEQ ID NO:452

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:452:

Glu Gln Val Gly Ala Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Asp
1 5 10 15

Ser Gln Ala Asp Ser Lys Glu Ala Glx Thr
20 25

(453) INFORMATION FOR SEQ ID NO:453

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:453:

Glu Gln Leu Gly Gly Leu Gln Pro Gly Arg Gly Thr Pro Gly Lys Val
1 5 10 15

Glu Gly Ser Val Glu Thr
20

(454) INFORMATION FOR SEQ ID NO:454

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:454:

10 Glu Gln Val Gly Ala Phe Gln Pro Gly Arg Gly Asn Ser Gly Lys Ala
1 5 10 15

15 Ser Lys Gly Asp Ser Lys Arg Pro Asp Thr
20 25

(455) INFORMATION FOR SEQ ID NO:455

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:455:

30 Glu Gln Val Gly Ala Phe Gln Pro Gly Lys Gly Asn Ser Gly Lys Ala
1 5 10 15

35 Ser Lys Gly Asp Ser Lys Arg Pro Asp Thr
20 25

(456) INFORMATION FOR SEQ ID NO:456

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:456:

50 Glu Gln Val Gly Ala Phe Gln Pro Gly Lys Gly Asn Ser Gly Lys Ala
1 5 10 15

55 Ser Lys Gly Asp Ser Asn Arg Pro Asp Thr
20 25

(457) INFORMATION FOR SEQ ID NO:457

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:457:

Gln Gln Val Gly Gly Val Gln Ala Gly Arg Ala Asn Pro Gly Lys Asp
1 5 10 15
Ser Arg Gly Ile Ser Lys Arg Thr Glu Thr
20 25

(458) INFORMATION FOR SEQ ID NO:458

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:458:

Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Lys Gln Gly Glu Ser Thr Arg Ser Glu Thr
20 25

(459) INFORMATION FOR SEQ ID NO:459

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:459:

Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Lys Gln Gly Thr Ser Thr Arg Ser Glu Thr
20 25

(460) INFORMATION FOR SEQ ID NO:460

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:460:

15 Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Lys Gln Gly Thr Ser Ala Arg Ser Glu Thr
20 25

20

(461) INFORMATION FOR SEQ ID NO:461

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:461:

35 Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15
Lys Gln Gly Thr Ser Ile Arg Ser Asp Thr
20 25

40

(462) INFORMATION FOR SEQ ID NO:462

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:462:

55

Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Glu
1 5 10 15

Lys Gln Gly Thr Ser Ile Arg Ser Asp Thr
20 25

(463) INFORMATION FOR SEQ ID NO:463

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:463:

Gln Gln Val Ala Glu Val Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
1 5 10 15

Asn Gln Gly Thr Ser Thr Arg Ser Asp Thr
20 25

(464) INFORMATION FOR SEQ ID NO:464

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:464:

Gln Gln Val Gly Glu Val Lys Pro Gly Arg Gly Thr Pro Gly Gln Gln
1 5 10 15

Lys Gln Asp Thr Ser Thr Arg Ser Asp Thr
20 25

(465) INFORMATION FOR SEQ ID NO:465

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:465:

5 Gln Gln Val Ala Glu Val Lys Pro Gly Arg Gly Thr Pro Gly His Pro
 1 5 10 15

10 Arg Gln Gly Ala Ser Phe Arg Ser Asp Ser
 20 25

(466) INFORMATION FOR SEQ ID NO:466

15 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

20 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:466:

25 Gln Gln Val Ser Glu Leu Lys Pro Gly Lys Gly Thr Pro Gly Gln Gln
 1 5 10 15

30 Gly Thr Gly Thr Ser Val Lys Ala Glu Thr
 20 25

(467) INFORMATION FOR SEQ ID NO:467

35 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
- (B) TYPE: amino acid
- (C) TOPOLOGY: linear

40 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:467:

45 Glu Gln Val Ala Glu Val Lys Pro Gly Lys Gly Ser Pro Gly Lys Pro
 1 5 10 15

50 Ser Gln Gly Lys Ser Ile Lys Ala Ser Thr
 20 25

(468) INFORMATION FOR SEQ ID NO:468

55 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids

EP 0 592 106 B1

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:468:

Glu Gln Val Ala Glu Val Lys Pro Gly Arg Gly Ser Pro Gly Lys Pro
1 5 10 15

Ser Gln Gly Lys Ser Ile Lys Ala Ser Thr
20 25

(469) INFORMATION FOR SEQ ID NO:469

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:469:

Gln Gln Val Ala Glu Val Lys Pro Gly Arg Gly Asp Pro Gly Arg Pro
1 5 10 15

Arg Gln Ala Ser Ser Thr Ile Ser Ala Thr
20 25

(470) INFORMATION FOR SEQ ID NO:470

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:470:

Glu Gln Val Ala Glu Val Pro Gln Gly Lys Gly Arg Pro Gly Lys Ser
1 5 10 15

Leu Gln Gly Lys Ser Leu Lys Ala Ser Thr
20 25

(471) INFORMATION FOR SEQ ID NO:471

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:471:

10 Gln Gln Met Ala Glu Val Lys Pro Gly Arg Gly Thr Pro Gly Lys Pro
1 5 10 15

15 Gly Val Val Pro Ser Phe Phe Ser Glu Thr
20 25

(472) INFORMATION FOR SEQ ID NO:472

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:472:

30 Gln Gln Val Ala Glu Val Lys Pro Gly Arg Gly Thr Pro Gly Arg Tyr
1 5 10 15

35 Ile Trp Glu Pro Ser Phe Phe Asn Glu Gly
20 25

(473) INFORMATION FOR SEQ ID NO:473

(i) SEQUENCE CHARACTERISTICS:

40 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:473:

50 Gln Gln Gln Ala Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Lys Pro
1 5 10 15

55 Ser Lys Ser Thr Ser Lys Thr Ala Ala Thr
20 25

(474) INFORMATION FOR SEQ ID NO:474

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:474:

10 Gln Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Lys Pro
1 5 10 15

15 Ser Lys Ser Thr Ser Lys Thr Ala Ala Thr
20 25

(475) INFORMATION FOR SEQ ID NO:475

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

25 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:475:

30 Gln Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Lys Pro
1 5 10 15

35 Ser Lys Ser Thr Ser Asn Thr Ala Ala Thr
20 25

(476) INFORMATION FOR SEQ ID NO:476

40 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

45 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:476:

50 Gln Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Ala Gly Lys Pro
1 5 10 15

55 Ser Lys Ser Thr Ser Lys Thr Ala Ala Thr
20 25

(477) INFORMATION FOR SEQ ID NO:477

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:477:

Arg Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Pro Pro Gly Lys Pro
1 5 10 15
Ser Arg Gly Thr Ser Arg Ser Ala Ala Thr
20 25

(478) INFORMATION FOR SEQ ID NO:478

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:478:

Gln Gln Gln Ala Gly Leu Lys Pro Ser Ser Gly Ser Pro Gly Arg Thr
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Ala Ala Thr
20 25

(479) INFORMATION FOR SEQ ID NO:479

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:479:

Gln Gln Glu Pro Gly Leu Arg Pro Ser Ser Gly Thr Pro Gly Arg Thr
1 5 10 15
Pro Arg Ser Thr Ser Lys Thr Ala Ala Thr
20 25

EP 0 592 106 B1

(480) INFORMATION FOR SEQ ID NO:480

(i) SEQUENCE CHARACTERISTICS:

5 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

10

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:480:

15 Xaa Gln Glu Pro Gly Leu Arg Pro Ser Ser Gly Ser Pro Gly Arg Thr
1 5 10 15
Pro Arg Ser Thr Ser Lys Thr Ala Ala Thr
20 25

20

(481) INFORMATION FOR SEQ ID NO:481

(i) SEQUENCE CHARACTERISTICS:

25 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:481:

35 Gln Gln Gln Pro Gly Leu Lys Pro Ser Ser Gly Ser Pro Ser Arg Val
1 5 10 15
Ser Lys Ser Thr Ser Lys Thr Pro Glu Thr
20 25

40

(482) INFORMATION FOR SEQ ID NO:482

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:482:

55

Gln His Gln Ala Gly Leu Lys Arg Ser Ser Gly Pro Pro Gly Lys Pro
1 5 10 15

Ser Thr Ser Thr Ser Lys Thr Ala Ala Thr
20 25

(483) INFORMATION FOR SEQ ID NO:483

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:483:

Glx Gln Glu Ser Gly Leu Lys Pro Thr Ser Gly Ser Pro Gly Lys Pro
1 5 10 15

Ser Lys Ser Arg Ser Lys Ala Ala Asp Ala
20 25

(484) INFORMATION FOR SEQ ID NO:484

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:484:

Gln Thr Lys Pro Thr Leu Lys Pro Thr Thr Gly Ser Pro Gly Arg Pro
1 5 10 15

Ser Lys Ser Thr Ser Lys Asp Pro Val Thr
20 25

(485) INFORMATION FOR SEQ ID NO:485

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:485:

5 Gln Thr Lys Pro Thr Leu Lys Pro Thr Thr Gly Ser Pro Gly Lys Pro
 1 5 10 15

Ser Arg Ser Thr Ser Arg Asp Pro Val Ser
 20 25

10 (486) INFORMATION FOR SEQ ID NO:486

(i) SEQUENCE CHARACTERISTICS:

15 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:486:

25

Glu Thr Arg Pro Ala Leu Lys Pro Thr Thr Gly Ser Pro Gly Lys Thr
1 5 10 15

Ser Lys Thr Thr Ser Lys Asp Pro Val Thr
20 25

(487) INFORMATION FOR SEQ ID NO:487

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:487:

45

Gln Asn Arg Pro Ala Leu Lys Ala Thr Thr Gly Ser Pro Gly Lys Thr
1 5 10 15

Ser Glu Thr Thr Ser Lys Asp Pro Ala Thr
20 25

(488) INFORMATION FOR SEQ ID NO:488

(i) SEQUENCE CHARACTERISTICS:

55 (A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:488:

Gln Thr Thr Pro Ala Leu Lys Pro Lys Thr Gly Ser Pro Gly Lys Thr
1 5 10 15

Ser Arg Thr Asp Ser Lys Asn Pro Val Thr
20 25

(489) INFORMATION FOR SEQ ID NO:489

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:489:

Gln Thr Arg Pro Ala Leu Arg Pro Thr Thr Gly Ser Pro Gly Glu Ala
1 5 10 15

Ser Glu Thr Thr Ser Lys Gly Pro Gly Thr
20 25

(490) INFORMATION FOR SEQ ID NO:490

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:490:

Gln Thr Arg Pro Ala Leu Lys Pro Thr Thr Gly Ser Pro Gly Lys Thr
1 5 10 15

Ser Glu Thr Thr Ser Arg Asp Thr Ala Tyr
20 25

(491) INFORMATION FOR SEQ ID NO:491

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 26 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:491:

5 Leu Glu Gly Val Gln Leu Trp Gly Gly Arg Gly Ile Ser Arg Lys Tyr
 1 5 10 15

Ala Lys Gly Asn Gly Lys Arg Glu Asp Ser
10 20 25

(492) INFORMATION FOR SEQ ID NO:492

15 (i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:492:

25

Tyr Asn Asn Pro Gly Asn Gly Tyr Ile Ala
1 5 10

30 (493) INFORMATION FOR SEQ ID NO:493

(i) **SEQUENCE CHARACTERISTICS:**

35 (A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:493:

Tyr Ile Asn Pro Gly Lys Gly Tyr Leu Ser
1 5 10

(494) INFORMATION FOR SEQ ID NO:494

(i) **SEQUENCE CHARACTERISTICS:**

50 (A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

55 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:494:

Arg Ala Ser Gln Glu Ile Ser Gly Tyr Leu Ser
1 5 10

5 (495) INFORMATION FOR SEQ ID NO:495

(i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:495:

Arg Ala Ser Gly Asn Ile His Asn Tyr Leu Ala
1 5 10

20

(496) INFORMATION FOR SEQ ID NO:496

25 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:496:

35

Arg Ala Ser Gln Asp Ile Asn Asn Phe Leu Asn
1 5 10

40

(497) INFORMATION FOR SEQ ID NO:497

(i) SEQUENCE CHARACTERISTICS:

45 (A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

50 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:497:

Arg Ala Ser Gln Ser Ile Gly Asn Asn Leu His
1 5 10

55

(498) INFORMATION FOR SEQ ID NO:498

(i) SEQUENCE CHARACTERISTICS:

EP 0 592 106 B1

(B) TYPE: amino acid

(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:498:

Ala Ala Ser Thr Leu Asp Ser
1 5

(499) INFORMATION FOR SEQ ID NO:499

(i) **SEQUENCE CHARACTERISTICS:**

(B) TYPE: amino acid

20 (C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:499:

Tyr Thr Thr Thr Leu Ala Asp
1 5

(500) INFORMATION FOR SEQ ID NO:500

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid

(ii) MOLECULE TYPE: peptide

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:500:

Phe Thr Ser Arg Ser Gln Ser
1 5

(501) INFORMATION FOR SEQ ID NO:501

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid

55 (C) TOPOLOGY: linear

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

EP 0 592 106 B1

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:501:

Lys Ala Ser Ser Leu Glu Ser
1 5

(502) INFORMATION FOR SEQ ID NO:502

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:502:

Leu Gln Tyr Leu Ser Tyr Pro Leu Thr
1 5

(503) INFORMATION FOR SEQ ID NO:503

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:503:

Gln His Phe Trp Ser Thr Pro Arg Thr
1 5

(504) INFORMATION FOR SEQ ID NO:504

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:504:

Gln Gln Gly Asn Ala Leu Pro Arg Thr
1 5

(505) INFORMATION FOR SEQ ID NO:505

EP 0 592 106 B1

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 7 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:505:

Gln Gln Tyr Asn Ser Tyr Ser
1 5

(506) INFORMATION FOR SEQ ID NO:506

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:506:

Thr Phe Gly Ile Thr
1 5

(507) INFORMATION FOR SEQ ID NO:507

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:507:

Gly Tyr Gly Val Asn
1 5

(508) INFORMATION FOR SEQ ID NO:508

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

EP 0 592 106 B1

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:508:

5

Ser Asn Gly Ile Asn
1 5

10

(509) INFORMATION FOR SEQ ID NO:509

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 5 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:509:

Asp Tyr Ala Met His
1 5

25

(510) INFORMATION FOR SEQ ID NO:510

(i) SEQUENCE CHARACTERISTICS:

30

(A) LENGTH: 10 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:510:

40

Glu Ile Phe Pro Gly Asn Ser Lys Thr Tyr
1 5 10

45

(511) INFORMATION FOR SEQ ID NO:511

(i) SEQUENCE CHARACTERISTICS:

50

(A) LENGTH: 9 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:511:

55

Met Ile Trp Gly Asp Gly Asn Thr Asp
1 5

5

(512) INFORMATION FOR SEQ ID NO:512

(i) SEQUENCE CHARACTERISTICS:

10

(A) LENGTH: 10 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

15

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:512:

Tyr Asn Asn Pro Gly Asn Gly Tyr Ile Ala
1 5 10

(513) INFORMATION FOR SEQ ID NO:513

(i) SEQUENCE CHARACTERISTICS:

25

(A) LENGTH: 9 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

30

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:513:

35

Ile Ser Trp Asp Ser Ser Ser Ile Gly
1 5

(514) INFORMATION FOR SEQ ID NO:514

(i) SEQUENCE CHARACTERISTICS:

40

(A) LENGTH: 5 amino acids
 (B) TYPE: amino acid
 (C) TOPOLOGY: linear

45

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:514:

50

Arg Glu Ile Arg Tyr
1 5

55

(515) INFORMATION FOR SEQ ID NO:515

(i) SEQUENCE CHARACTERISTICS:

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(A) LENGTH: 8 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

5 (ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:515:

10 **Glu Arg Asp Tyr Arg Leu Asp Tyr**
1 5

15

(516) INFORMATION FOR SEQ ID NO:516

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 12 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:516:

30 **Ser Glu Tyr Tyr Gly Gly Ser Tyr Lys Phe Asp Tyr**
1 5 10

(517) INFORMATION FOR SEQ ID NO:517

35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 17 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

40

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:517:

45

Gly Arg Asp Tyr Tyr Asp Ser Gly Gly Tyr Phe Thr Val Ala Phe Asp
1 5 10 15

50 **Ile**
:

(518) INFORMATION FOR SEQ ID NO:518

55 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 11 amino acids
(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:518:

Arg Ala Ser Gln Ser Ile Ser Arg Trp Leu Ala
 1 5 10

10

(519) INFORMATION FOR SEQ ID NO:519

(i) SEQUENCE CHARACTERISTICS:

15

(A) LENGTH: 7 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:519:

25

Glu Ala Ser Asn Asp Leu Ala
 1 5

(520) INFORMATION FOR SEQ ID NO:520

30

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 5 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

35

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:520:

40

Asp Phe Tyr Met Glu
 1 5

(521) INFORMATION FOR SEQ ID NO:521

45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 9 amino acids

(B) TYPE: amino acid

(C) TOPOLOGY: linear

50

(ii) MOLECULE TYPE: peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:521:

55

Ile Ile Trp Asp Asp Gly Ser Asp Gln
 1 5

5 (A) LENGTH: 11 amino acids
(B) TYPE: amino acid
(C) TOPOLOGY: linear

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- (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;

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- 40

- (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent variable region;

- 45

- (i) producing said paired peptides,

- 55

- 219

3. The method of claim 1 or 2, wherein the variable region of the rodent antibody is a variable region of a murine antibody.
4. The method of claim 1 or 2, wherein said surface exposed amino acid residues are those residues whose solvent accessibility is above 30%.
5. A peptide obtained by the method of any one of claims 1 to 4.
6. A method of producing a humanized rodent antibody or fragment thereof by resurfacing, said method comprising:
 - (a) generating sequence alignments, in framework positions only, from relative accessibility distributions from x-ray crystallographic structures of a pool of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions;
 - (b) defining for a rodent antibody or fragment thereof a set of variable region heavy and light chain surface exposed amino acid residues using said set of surface exposed framework positions generated in said step (a);
 - (c) identifying from human antibody amino acid sequences a set of variable region heavy and light chain surface exposed amino acid residues that is most closely identical to said set of rodent surface exposed amino acid residues defined in said step (b), wherein said heavy and light chains from said human antibody are or are not naturally paired;
 - (d) substituting, in the amino acid sequence of said rodent antibody or fragment thereof, said set of heavy and light chain surface exposed amino acid residues defined in said step (b) with said human set of heavy and light chain surface exposed amino acid residues identified in said step (c);
 - (e) constructing three-dimensional models of said variable region of said rodent antibody or fragment thereof and of said variable region of said rodent antibody or fragment thereof resulting from the substituting specified in said step (d);
 - (f) comparing said three-dimensional models constructed in said step (e) and identifying any amino acid residues from said sets identified in said steps (b) and (c) that are close to any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof;
 - (g) changing any residues identified in said step (f) from the human to the original rodent amino acid residue to thereby define a humanizing set of surface exposed amino acid residues;
 - (h) replacing the set of rodent antibody surface exposed amino acid residues defined in said step (b) with the humanizing set of surface exposed amino acid residues defined in said step (g); and
 - (i) producing said humanized antibody or fragment thereof,

characterized in that in step (a) sequence alignments are generated from a sufficient number of antibody variable region heavy and light chains to give a set of heavy and light chain surface exposed framework positions wherein said set is identical in at least 98% of said sequence alignment positions and **in that** in step (f) amino acid residues from said sets identified in said steps (b) and (c) that are within $5 \times 10^{-10} \text{m}$ (5 Ångstroms) of any atom of any residue of the complementarity determining regions of said rodent antibody or fragment thereof to be humanized are identified.
7. The method of claim 6, wherein said rodent antibody is an antibody fragment.
8. The method of claim 6 or 7, wherein the set of heavy and light chain surface exposed framework positions in step (a) is identical in at least 98% of said sequence alignment positions.
9. The method of claim 7, wherein said rodent antibody fragment is a single chain antibody, a F_v fragment, a Fab fragment, a Fab_2 fragment or a Fab fragment.
10. The method of claim 6, 7 or 8, wherein said step (c) identifies a set of naturally paired heavy and light chain surface exposed amino acid residues that is most closely identical to said set of surface exposed amino acid residues defined in said step (b).
11. The method of claim 6, 7 or 8, wherein said surface exposed amino acid residues are those residues whose solvent accessibility is 30%.
12. The method of claim 6, 7 or 8, wherein the rodent antibody or fragment thereof is a murine antibody.

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13. The method of claim 12, wherein said set of framework positions of surface exposed amino acid residues is defined by the set shown in Table 1 and the alignments set forth in Figures 3A and 3B:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 O 24 S 24 Y 6	V 83 Q 22 L 5
5 9	T 61 L 37 P 26 S 26 G 17 A 14 L 7	T 87 S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 O 12 T 8
46	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 87 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 8
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 69 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 O 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 O 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 85 I 8 T 8 R 5	S 48 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 6	E 66 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43

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Table 1 (continued)

Heavy Chain		
Position	Human	Mouse
212	T 91	

14. The method of claim 6, 7 or 8 wherein the rodent antibody or fragment thereof is murine antibody N901.

15. The method of claim 14, wherein said set of framework positions of surface exposed amino acid residues is defined by the set shown in Table 1 and the alignments set forth in Figures 3A and 3B:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 78 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T B7
9	P 26 S 26 G 17 A 14 L,7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28
73	S 96	S 90 I 5
76	D 43 T 16 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T B	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 8 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
116	E 47 Q 46	E 59 Q 29 D 10
120	Q 63 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 8
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 17

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Table 1 (continued)

Heavy Chain		
Position	Human	Mouse
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 5
196	S 91	S 76 A 16
197	K 85 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

16. A resurfaced rodent antibody or fragment thereof made by the method of claim 6, 7 or 8.

17. The resurfaced antibody or fragment thereof of claim 16, wherein said rodent antibody is an antibody fragment.

18. The resurfaced antibody or fragment thereof of claim 17, wherein said rodent antibody fragment is a single chain antibody, a F_v fragment, a Fab fragment, a Fab₂ fragment or a Fab fragment.

19. The resurfaced antibody or fragment thereof of claim 16 or 17, wherein said surface exposed amino acid residues are those residues whose solvent accessibility is above 30%.

20. The resurfaced antibody or fragment thereof of claim 16 or 17, wherein the rodent antibody or fragment thereof is a murine antibody.

21. The resurfaced antibody or fragment thereof of claim 20, wherein said set of framework positions of surface exposed amino acid residues is defined by the set shown in Table 1 and the alignments set forth in Figures 3A and 3B:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T 67
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5

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Table 1 (continued)

Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 64 S 10	P 69 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 6	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
206	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

22. The resurfaced antibody or fragment thereof of claim 16 or 17, wherein the rodent antibody or fragment thereof to be humanized is murine antibody N901.

23. The resurfaced antibody or fragment thereof of claim 16 or 17, wherein said framework positions of surface exposed amino acid residues is defined by the set shown in Table I and the alignments set forth in Figures 3A and 3B:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 I L 37	T 87
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26

Table 1 (continued)

Light Chain		
Position	Human	Mouse
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 66 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	Q 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 6
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 6 V 5	T 53 S 43
212	T 91	

Patentansprüche

1. Verfahren zur Erzeugung eines Antikörpers oder eines Fragments hiervon, der humanisierte schwere und leichte Ketten der variablen Region eines Nagetierantikörpers umfasst, wobei das Verfahren folgendes umfasst:

(a) Erzeugen von Sequenzalignments, lediglich in Gerüst- (Framework-) Positionen, aus relativen Zugänglichkeitsverteilungen aus Röntgenkristallographiestrukturen eines Pooles schwerer und leichter Ketten der variablen Antikörperregion, um einen Satz schwerer und leichter Ketten oberflächenexponierten Gerüst-Positionen zu ergeben;

(b) Bestimmen eines Satzes schwerer und leichter Ketten oberflächenexponierter Aminosäurereste für die variable Region eines Nagetierantikörpers unter Verwendung des Satzes an oberflächenexponierten Gerüst-

Positionen, erzeugt in Schritt (a);

(c) Identifizieren eines Satzes schwerer und leichter Ketten oberflächenexponierter Aminosäurereste einer variablen Region, die denjenigen des Satzes der Nagetieroberflächenexponierten Aminosäurereste, definiert in Schritt (b), am ähnlichsten ist, aus Aminosäuresequenzen eines humanen Antikörpers, wobei die schweren und leichten Ketten dieses humanen Antikörpers natürlich gepaart sind oder nicht natürlich gepaart sind;

(d) Substituieren in der Aminosäuresequenz der variablen Nagetier-Region des Satzes an schweren und leichten Ketten oberflächenexponierten Aminosäureresten, definiert in Schritt (b), durch den humanen Satz an schweren und leichten Ketten oberflächenexponierten Aminosäureresten identifiziert in Schritt (c);

(e) Konstruieren dreidimensionaler Modelle der variablen Region des Nagetierantikörpers und der variablen Region des Nagetierantikörpers, die sich durch das Substituieren ergibt, das in Schritt (d) spezifiziert ist;

(f) Vergleichen der dreidimensionalen Modelle, die in Schritt (e) konstruiert wurden und Identifizieren aller Aminosäurereste aus den in den Schritten (b) und (c) identifizierten Sätzen, die jedem Atom jedes Restes der komplementaritätsbestimmenden Regionen der variablen Nagetier-Regionen nahe ist;

(g) Verändern aller in Schritt (f) identifizierten Reste vom humanen zum ursprünglichen Nagetieraminosäurerest, um dadurch einen humanisierenden Satz an oberflächenexponierten Aminosäureresten zu definieren;

(h) Ersetzen des Satzes der variablen Region oberflächenexponierter Aminosäurereste eines Nagetierantikörpers definiert in Schritt (b) durch den humanisierenden Satz an oberflächenexponierten Aminosäureresten definiert in Schritt (g); und

(i) Erzeugen der gepaarten Peptide,

dadurch gekennzeichnet, dass in Schritt (a) Sequenzalignments aus einer ausreichenden Anzahl schwerer und leichter Ketten aus variablen Antikörper-Regionen erzeugt werden, um einen Satz an schweren und leichten Ketten oberflächenexponierten Gerüst-Positionen zu liefern, wobei der Satz in zumindest 98% des Sequenzalignmentspositionen identisch ist und dadurch, dass in Schritt (f) Aminosäurereste aus diesen in Schritten (b) und (c) identifizierten Sätzen, die innerhalb 5×10^{-10} m (5 Ångström) jedes Atoms jedes Restes der komplementaritätsbestimmenden Regionen der variablen Region liegen, die humanisiert werden sollen, identifiziert werden.

2. Verfahren nach Anspruch 1, wobei der Satz oberflächenexponierter Gerüst-Positionen der schweren und leichten Ketten in Schritt (a) in zumindest 98% der Sequenzalignmentspositionen identisch ist.

3. Verfahren nach Anspruch 1 oder 2, wobei die variable Region des Nagetierantikörpers eine variable Region eines murinen Antikörpers ist.

4. Verfahren nach Anspruch 1 oder 2, wobei die oberflächenexponierten Aminosäurereste solche Reste sind, deren Lösungsmittelzugänglichkeit über 30% ist.

5. Peptid, das durch das Verfahren nach einem der Ansprüche 1 - 4 erhältlich ist.

6. Verfahren zur Herstellung eines humanisierten Nagetierantikörpers oder Fragmentes hiervon durch Umgestalten der Oberfläche, wobei das Verfahren folgendes umfasst:

(a) Erzeugen von Sequenzalignments, nur in Gerüst-Positionen, aus den relativen Zugänglichkeitsverteilungen aus Röntgenkristallographiestrukturen eines Pooles schwerer und leichter Ketten von variablen Antikörperregionen, um einen Satz an leichten und schweren Ketten oberflächenexponierten Gerüst-Positionen zu liefern;

(b) Definieren für einen Nagetierantikörper oder Fragment hiervon eines Satzes schwerer und leichter Ketten oberflächenexponierter Aminosäurereste variabler Regionen unter Verwendung des Satzes an oberflächenexponierten Gerüst-Positionen, die in Schritt (a) erzeugt wurden;

(c) Identifizieren eines Satzes schwerer und leichter Ketten oberflächenexponierter Aminosäurereste einer variablen Region aus humanen Antikörperaminosäuresequenzen, die dem Satz an oberflächenexponierten Nagetier-Aminosäureresten definiert in Schritt (b) am meisten identisch sind, wobei die schweren und leichten Ketten aus dem humanen Antikörper natürlich gepaart oder nicht gepaart sind;

(d) Substituieren in der Aminosäuresequenz des Nagetierantikörpers oder Fragments hiervon des Satzes aus schweren und leichten Ketten oberflächenexponierten Aminosäureresten definiert in Schritt (b) mit dem humanen Satz an schweren und leichten Ketten oberflächenexponierten Aminosäureresten identifiziert in Schritt (c);

(e) Konstruieren dreidimensionaler Modelle der variablen Region des Nagetierantikörpers oder des Fragments hiervon und der variablen Region des Nagetierantikörpers oder Fragments hiervon, der sich aus dem in Schritt

(d) spezifizierten Substituieren ergibt;

(f) Vergleichen der dreidimensionalen Modelle, die in Schritt (e) konstruiert wurden und Identifizieren aller Aminosäurereste aus den in den Schritten (b) und (c) identifizierten Sätzen, die jedem Atom oder jedem Rest der komplementaritätsbestimmenden Regionen des Nagetierantikörpers oder Fragments hiervon ähnlich sind;

(g) Verändern aller Reste, die in Schritt (f) identifiziert wurden, vom humanen zum ursprünglichen Nagetieraminosäurerest, um dadurch einen humanisierenden Satz an oberflächenexponierten Aminosäureresten zu definieren;

(h) Ersetzen des Satzes an Nagetierantikörper oberflächenexponierten Aminosäureresten definiert in Schritt (b) durch den humanisierenden Satz an oberflächenexponierten Aminosäureresten definiert in Schritt (g); und

(i) Erzeugen des humanisierten Antikörpers oder Fragments hiervon;

dadurch gekennzeichnet, dass in Schritt (a) Sequenzalignments aus einer ausreichenden Anzahl an schweren und leichten Ketten der variablen Antikörper-Region erzeugt werden, um einen Satz an schweren und leichten Ketten oberflächenexponierten Gerüst-Positionen zu liefern, wobei der Satz in zumindest 98% der Sequenzalignmentspositionen identisch ist und

dadurch gekennzeichnet, dass in Schritt (f) Aminosäurereste aus den in den Schritten (b) und (c) identifizierten Aminosäureresten, die innerhalb 5×10^{-10} m (5 Ångström) von jedem Atom jedes Restes der komplementaritätsbestimmenden Regionen des Nagetierantikörpers oder Fragments hiervon, die humanisiert werden sollen, liegen, identifiziert werden.

7. Verfahren nach Anspruch 6, wobei der Nagetierantikörper ein Antikörperfragment ist.
8. Verfahren nach Anspruch 6 oder 7, wobei der Satz an schweren und leichten Ketten oberflächenexponierten Gerüst-Positionen in Schritt (a) in zumindest 98% des Sequenzalignmentspositionen identisch sind.
9. Verfahren nach Anspruch 7, wobei das Nagetierantikörperfragment ein einkettiger Antikörper, ein F_v -Fragment, ein Fab-Fragment, ein Fab_2 -Fragment oder ein Fab'-Fragment ist.
10. Verfahren nach Anspruch 6, 7 oder 8, wobei Schritt (c) einen Satz natürlich gepaarter schwerer und leichter Ketten oberflächenexponierter Aminosäurereste identifiziert, die zu dem Satz an oberflächenexponierten Aminosäureresten, definiert in Schritt (b), am meisten identisch sind.
11. Verfahren nach Anspruch 6, 7 oder 8, wobei die oberflächenexponierten Aminosäurereste solche Reste sind, deren Lösungsmittelzugänglichkeit 30% beträgt.
12. Verfahren nach Anspruch 6, 7 oder 8, wobei der Nagetierantikörper oder das Fragment hiervon ein muriner Antikörper ist.
13. Verfahren nach Anspruch 12, wobei der Satz an Gerüst-Positionen oberflächenexponierter Aminosäurereste durch den in Tabelle 1 dargestellten Satz und die Alignments definiert ist, die in den Figuren 3A und 3B dargelegt sind.

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 83 Q 22 L 5
5 9	T 61 L 37 P 26 S 26 G 17 A 14 L 7	T 87 S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 8
46	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28
73	S 96	S 90 I 5

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Table 1 (fortgesetzt)

Light Chain		
Position	Human	Mouse
76	D 43 T 18 S 16 E 15	D 87 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 8
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 69 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 85 I 8 T 8 R 5	S 48 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 6	E 66 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

14. Verfahren nach Anspruch 6, 7 oder 8, wobei der Nagetierantikörper oder das Fragment hiervon der murine Antikörper N901 ist.

15. Verfahren nach Anspruch 14, wobei der Satz an Gerüst-Positionen oberflächenexponierter Aminosäurereste durch den in Tabelle 1 dargestellten Satz und die in den Figuren 3A und 3B dargelegten Alignments definiert ist.

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 78 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5

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Table 1 (fortgesetzt)

Light Chain		
Position	Human	Mouse
5	T 61 L 37	T B7
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
10	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28
15	S 96	S 90 I 5
76	D 43 T 16 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T B	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
20	111 K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 8 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
25	116 E 47 Q 46	E 59 Q 29 D 10
120	Q 63 T 7	Q 68 K 26
30	122 V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
35	131 P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
40	145 T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 8
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 17
45	184 S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 5
196	S 91	S 76 A 16
50	197 K 85 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
55	212 T 91	

16. Ein in seiner Oberfläche umgeformter Nagetierantikörper oder ein Fragment hiervon, der durch das Verfahren nach Anspruch 6, 7 oder 8 hergestellt wurde.

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17. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 16, wobei der Nagetierantikörper ein Antikörperfragment ist.
18. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 17, wobei das Nagetierantikörperfragment ein einkettiger Antikörper, ein F_v-Fragment, ein Fab-Fragment, ein Fab₂-Fragment oder ein Fab'-Fragment ist.
19. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 16 oder 17, wobei die oberflächenexponierten Aminosäurereste solche Reste sind, deren Lösungsmittelzugänglichkeit über 30% beträgt.
20. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 16 oder 17, wobei der Nagetierantikörper oder das Fragment hiervon ein muriner Antikörper ist.
21. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 20, wobei der Satz an Gerüst-Positionen oberflächenexponierter Aminosäurereste durch den in Tabelle 1 dargestellten Satz und die in den Figuren 3A und 3B dargelegten Alignments definiert ist:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T 67
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98

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Table 1 (fortgesetzt)

Heavy Chain		
Position	Human	Mouse
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 64 S 10	P 69 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 6	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
206	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

22. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 16 oder 17, wobei der Nagetierantikörper oder das Fragment hiervon, das humanisiert werden soll, der murine Antikörper N901 ist.

23. Oberflächenumgeformter Antikörper oder Fragment hiervon nach Anspruch 16 oder 17, wobei die Gerüst-Positionen oberflächenexponierter Aminosäurereste durch den in Tabelle 1 dargestellten Satz und die in den Figuren 3A und 3B dargelegten Alignments definiert ist:

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 I L 37	T 87
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5

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Table 1 (fortgesetzt)

Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 66 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	Q 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 6
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 6 V 5	T 53 S 43
212	T 91	

Revendications

1. Procédé pour produire un anticorps ou un fragment de celui-ci qui comprend des chaînes lourdes et légères humanisées d'une région variable d'un anticorps de rongeur, ledit procédé comprenant :

(a) la réalisation d'alignement de séquences, dans des positions de structure uniquement, à partir de distribution par approche relative de structure cristallographique au rayon X d'un ensemble de chaînes lourdes et légères d'une région variable d'anticorps pour donner un jeu de position de structure exposé à la surface d'une chaîne lourde et légère;

(b) la définition pour une région variable d'anticorps de rongeur d'un jeu de résidus d'acide aminé exposé à la surface de chaînes lourdes et légères en utilisant ledit jeu de position de structure exposé à la surface réalisé dans ladite étape (a) ;

(c) l'identification à partir de séquences d'acides aminés d'anticorps humains d'un jeu de résidus d'acides aminés exposés à la surface de chaîne lourde et légère de région variable qui est le plus strictement identique audit jeu de résidus d'acides aminés exposés à la surface de rongeurs définis dans ladite étape (b), dans lequel lesdites chaînes lourdes et légères dudit anticorps humain sont ou ne sont pas naturellement appariées ;

(d) la substitution dans la séquence d'acides aminés de ladite région variable de rongeurs, dudit jeu de résidus d'acide aminés exposés à la surface de chaînes lourdes et légères défini dans ladite étape (b) avec ledit jeu humain de résidus d'acides aminés exposés à la surface de chaînes lourdes et légères identifié dans ladite étape (c) ;

(e) la construction de modèles tridimensionnels de ladite région variable dudit anticorps de rongeur et de ladite région variable dudit anticorps de rongeurs résultant de la substitution spécifiée dans ladite étape (d);

(f) la comparaison desdits modèles tridimensionnels construits dans ladite étape (e) et l'identification de tout

résidus d'acides aminés à partir desdits jeux identifiés dans lesdites étapes (b) et (c) qui sont proches de tout atome de tout résidus des régions de détermination complémentaires de ladite région variable de roneurs ;
 (g) le changement de tout résidus identifié dans ladite étape (f) du résidu d'acide aminé humain au résidu d'acide aminé de roneurs pour ainsi définir un jeu humanisant de résidus d'acides aminés exposés à la surface ;

(h) le remplacement du jeu de résidus d'acides aminés exposé à la surface de la région variable d'anticorps de roneurs défini dans ladite étape (b) avec le jeu humanisant de résidus d'acides aminés exposés à la surface définie dans ladite étape (g) ; et

(i) la production de peptides apparées,

caractérisé en ce que dans l'étape (a), les alignements de séquences sont réalisés à partir d'un nombre suffisant de chaînes lourdes et légères de régions variables d'anticorps pour donner un jeu de positions de structure exposé à la surface de chaînes lourdes et légères dans lesquelles ledit jeu est identique dans au moins 98% desdites positions d'alignement de séquences et **en ce que** dans l'étape (f), les résidus d'acides aminés à partir desdits jeux identifiés dans lesdites étapes (b) et (c) qui sont de $5 \times 10^{-10} \text{m}$ (5 Ångströms) de tout atome de tout résidus des régions de détermination complémentaires de ladite région variable à humaniser sont identifiés.

2. Procédé selon la revendication 1, dans lequel le jeu de positions de structure exposé à la surface de chaînes lourdes et légères dans l'étape (a) est identique à au moins 98% desdites positions d'alignement de séquences.

3. Procédé selon la revendication 1 ou 2, dans lequel la région variable de l'anticorps de roneurs est une région variable d'un anticorps de murin.

4. Procédé selon la revendication 1 ou 2, dans lequel lesdits résidus d'acides aminés exposés à la surface sont des résidus dont l'accessibilité au solvant est au-dessus de 30%.

5. Peptide obtenu par le procédé selon l'une quelconque des revendications 1 à 4.

6. Procédé de production d'un anticorps de roneurs humanisés ou d'un fragment de celui-ci par remodelage de la surface, ledit procédé comprenant :

(a) la réalisation d'alignement de séquences, dans des positions de structure uniquement, à partir de distribution par approche relative de structure cristallographique au rayon X d'un ensemble de chaînes lourdes et légères de régions variables d'anticorps pour donner un jeu de position de structure exposé à la surface de chaînes lourdes et légères ;

(b) la définition pour un anticorps de roneurs ou pour un fragment de celui-ci d'un jeu de résidus d'acide aminé exposé à la surface de chaînes lourdes et légères de région variable en utilisant ledit jeu de positions de structure exposé à la surface réalisé selon ladite étape (a) ;

(c) l'identification à partir de séquences d'acides aminés d'anticorps humains d'un jeu de résidus d'acides aminés exposés à la surface de chaînes lourdes et légères de régions variables qui est le plus strictement identique audit jeu de résidus d'acides aminés exposés à la surface de roneurs définis dans ladite étape (b), dans lequel lesdites chaînes lourdes et légères dudit anticorps humain sont ou ne sont pas naturellement apparées ;

(d) la substitution dans la séquence d'acides aminés dudit anticorps de roneurs ou d'un fragment de celui-ci dudit jeu de résidus d'acides aminés exposés à la surface de chaînes lourdes et légères défini dans ladite étape (b) avec ledit jeu humain de résidus d'acides aminés exposés à la surface de chaînes lourdes et légères identifié dans ladite étape (c) ;

(e) la construction de modèles tridimensionnels de ladite région variable dudit anticorps de roneur ou d'un fragment de celui-ci et de ladite région variable dudit anticorps de roneurs ou d'un fragment de celui-ci résultant de la substitution spécifiée dans ladite étape (d) ;

(f) la comparaison desdits modèles tridimensionnels construits dans ladite étape (e) et l'identification de tout résidus d'acides aminés à partir desdits jeux identifiés dans lesdites étapes (b) et (c) qui sont proches de tout atome de tout résidus des régions de détermination complémentaires dudit anticorps de roneurs ou d'un fragment de celui-ci ;

(g) le changement de tout résidus identifié dans ladite étape (f) du résidu d'acide aminé humain en un résidu d'acides aminés de roneurs d'origine pour ainsi définir un jeu humanisant de résidus d'acides aminés exposés à la surface ;

(h) le remplacement du jeu de résidus d'acides aminés exposé à la surface d'anticorps de roneurs définie

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dans ladite étape (b) avec le jeu humanisant de résidus d'acides aminés exposés à la surface définie dans ladite étape (g) ; et

(i) la production dudit anticorps humanisé ou d'un fragment de celui-ci,

- 5 **caractérisé en ce que** dans l'étape (a) les alignements de séquences sont réalisés à partir d'un nombre suffisant de chaînes lourdes et légères de régions variables d'anticorps pour donner un jeu de positions de structure exposé à la surface de chaînes lourdes et légères dans lequel ledit jeu est identique dans au moins 98% desdites positions d'alignement de séquences et **en ce que** dans l'étape (f), les résidus d'acides aminés à partir des jeux identifiés dans
- 10 lesdites étapes (b) et (c) qui sont de $5 \times 10^{-10} \text{m}$ (5 Ångströms) de tout atome de tout résidu des régions de détermination complémentaires dudit anticorps de rongeurs ou d'un fragment de celui-ci à humaniser sont identifiés.
7. Procédé selon la revendication 6, dans lequel ledit anticorps de rongeurs est un fragment d'anticorps.
8. Procédé selon la revendication 6 ou 7, dans lequel le jeu de positions de structure exposé à la surface de chaînes
- 15 lourdes et légères dans l'étape (a) est identique à au moins 98% desdites positions d'alignement de séquences.
9. Procédé selon la revendication 7, dans lequel ledit fragment d'anticorps de rongeurs est un anticorps à chaîne unique, un fragment F_v , un fragment F_{ab} , un fragment F_{ab_2} ou un fragment F_{ab}' .
- 20 10. Procédé selon la revendication 6, 7 ou 8, dans lequel ladite l'étape (c) identifie un jeu de résidus d'acides aminés exposés à la surface de chaînes lourdes et légères naturellement appariées qui est le plus strictement identique audit jeu de résidus d'acides aminés exposés à la surface définie dans ladite étape (b).
11. Procédé selon la revendication 6, 7 ou 8, dans lequel lesdits résidus d'acides aminés exposés à la surface sont
- 25 des résidus dont l'accessibilité par solvant est de 30%.
12. Procédé selon la revendication 6, 7 ou 8, dans lequel l'anticorps de rongeurs ou un fragment de celui-ci est un anticorps murin.
- 30 13. Procédé selon la revendication 12, dans lequel ledit jeu des positions de structure des résidus d'acides aminés exposés à la surface est défini par le jeu représenté dans le tableau 1 et les alignements établis sur les figures 3A et 3B :

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 83 Q 22 L 5
5 9	T 61 L 37 P 26 S 26 G 17 A 14 L 7	T 87 S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 8
46	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 87 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 8
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 69 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5

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Table 1 (suite)

Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 85 I 8 T 8 R 5	S 48 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 6	E 66 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

14. Procédé selon la revendication 6, 7 ou 8, dans lequel l'anticorps de rongeurs ou un fragment de celui-ci est un anticorps murin N901.

15. Procédé selon la revendication 14, dans lequel ledit jeu de positions de structure des résidus d'acides aminés exposés à la surface est défini par le jeu représenté dans le tableau 1 et les alignements établis sur les figures 3A et 3B :

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 78 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T B7
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 62 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 28

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Table 1 (suite)

Light Chain		
Position	Human	Mouse
73	S 96	S 90 I 5
76	D 43 T 16 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T B	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 8 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
116	E 47 Q 46	E 59 Q 29 D 10
120	Q 63 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 8
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 17
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 5
196	S 91	S 76 A 16
197	K 85 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

16. Anticorps de rongeurs remodelé à la surface ou fragment de celui-ci réalisé par le procédé de la revendication 6, 7 ou 8.

17. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 16, dans lequel ledit anticorps de rongeurs est un fragment d'anticorps.

18. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 17, dans lequel ledit fragment d'anticorps de rongeurs est un anticorps à chaîne unique, un fragment F_v , un fragment Fab, un fragment Fab_2 ou un fragment Fab'.

19. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 16 ou 17, dans lequel lesdits résidus

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d'acides aminés exposés à la surface sont des résidus dont l'accessibilité par solvant est au-dessus de 30%.

20. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 16 ou 17, dans lequel l'anticorps de rongeurs ou un fragment de celui-ci est un anticorps murin.

21. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 20, dans lequel ledit jeu de positions de structure des résidus d'acides aminés exposés à la surface est défini par le jeu représenté dans le tableau 1 et les alignements établis sur les figures 3A et 3B :

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 L 37	T 67
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 68 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	G 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 81 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 68 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 64 S 10	P 69 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 6	K 50 Q 30 N 10 H 5
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7

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Table 1 (suite)

Heavy Chain		
Position	Human	Mouse
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
206	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 8 V 5	T 53 S 43
212	T 91	

22. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 16 ou 17, dans lequel l'anticorps de rongeurs ou un fragment de celui-ci à humaniser est un anticorps murin N901.

23. Anticorps remodelé à la surface ou fragment de celui-ci selon la revendication 16 ou 17, dans lequel lesdites positions de structure des résidus d'acides aminés exposés à la surface sont définies par le jeu représenté dans le tableau 1 et les alignements établis sur les figures 3A et 3B :

Table 1

Light Chain		
Position	Human	Mouse
1	D 51 E 34 A 5 S 5	D 76 Q 9 E 6
3	V 38 Q 24 S 24 Y 6	V 63 Q 22 L 5
5	T 61 I L 37	T 87
9	P 26 S 26 G 17 A 14 L 7	S 36 A 29 L 17 P 5
15	P 62 V 25 L 12	L 47 P 30 V 8 A 7
18	R 57 S 18 T 13 P 6	R 38 K 22 S 13 Q 12 T 9
46	P 94	P 82 S 9
47	G 89	G 71 D 18
51	K 43 R 31	K 70 Q 13 R 8 T 5
63	G 91	G 98
66	D 43 S 25 A 9	D 38 A 26 S 26
73	S 96	S 90 I 5
76	D 43 T 18 S 16 E 15	D 67 S 15 A 5 K 5
86	P 44 A 27 S 17 T 8	A 50 P 11 T 8 E 7 Q 6
87	E 71 D 11 G 7	E 91 D 6
111	K 74 R 12 N 6	K 93
115	K 54 L 40	K 87 L 5
116	R 60 G 33 S 5	R 89 G 9
117	Q 50 T 37 E 6 P 6	A 74 Q 14 P 5 R 5
Heavy Chain		
Position	Human	Mouse
118	E 47 Q 46	E 59 Q 29 D 10
120	Q 83 T 7	Q 66 K 26
122	V 59 L 15 Q 13	Q 57 V 27 L 5 K 5
126	G 54 A 23 P 18	G 36 P 30 A 29
127	Q 53 E 22 A 14 D 7	E 45 G 43 S 6
128	L 61 V 31 F 7	L 96
130	K 46 Q 41 E 5	K 52 Q 27 R 17

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Table 1 (suite)

Heavy Chain		
Position	Human	Mouse
131	P 95	P 91 A 5
132	G 74 S 16 T 7	G 82 S 17
136	R 53 K 23 S 17 T 7	K 66 S 17 R 13
143	G 96	G 98
145	T 46 S 32 N 9 I 7	T 63 S 19 N 7 A 5 D 5
160	P 84 S 10	P 89 H 7
161	G 93	G 71 E 24
162	K 76 Q 10 R 8	K 50 Q 30 N 10 H 6
183	D 26 P 25 A 17 Q 10 T 7	E 31 P 22 D 17 A 12 Q 11
184	S 70 K 9 P 8	K 42 S 37 T 6
186	K 53 Q 22 R 7 N 5	K 83 Q 7
187	G 66 S 21 T 5	G 62 S 18 D 10
195	T 30 D 26 N 19 K 7	T 36 K 30 N 26 D 6
196	S 91	S 76 A 16
197	K 65 I 8 T 8 R 5	S 46 K 34 Q 11
208	R 46 T 18 K 17 D 6	S 67 A 14 T 11
209	A 50 P 21 S 13 T 8	E 88 D 7
210	E 46 A 18 D 13 S 9 Z 6 V 5	T 53 S 43
212	T 91	

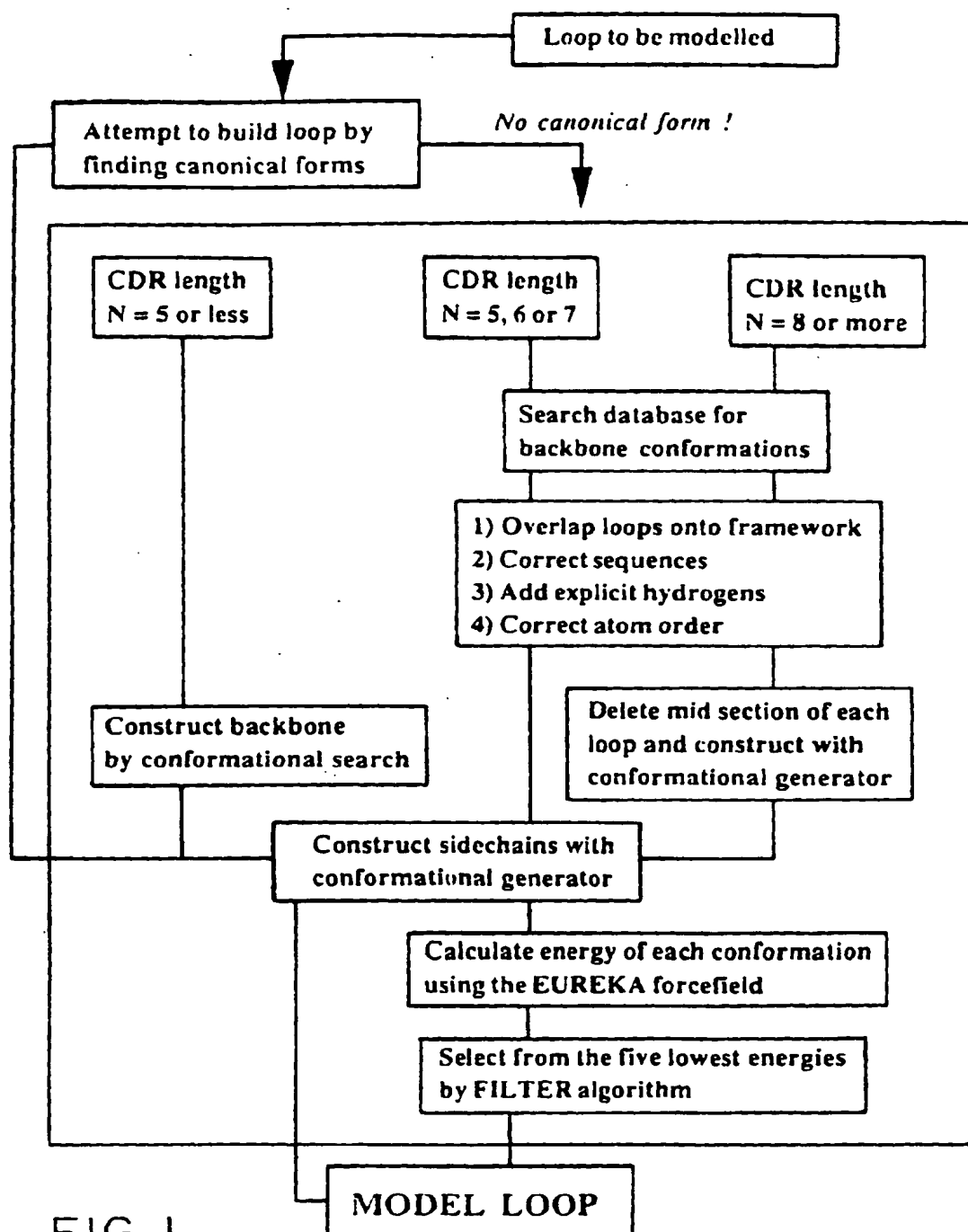


FIG. 1

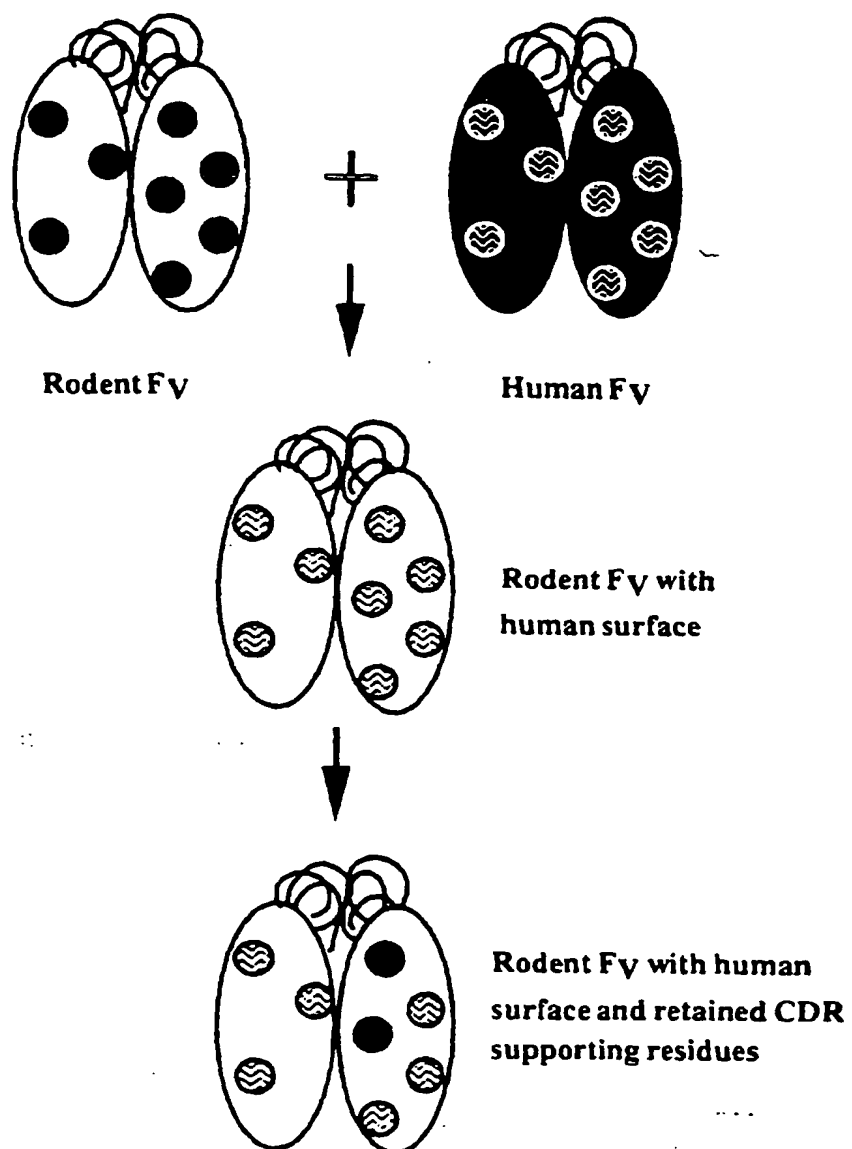
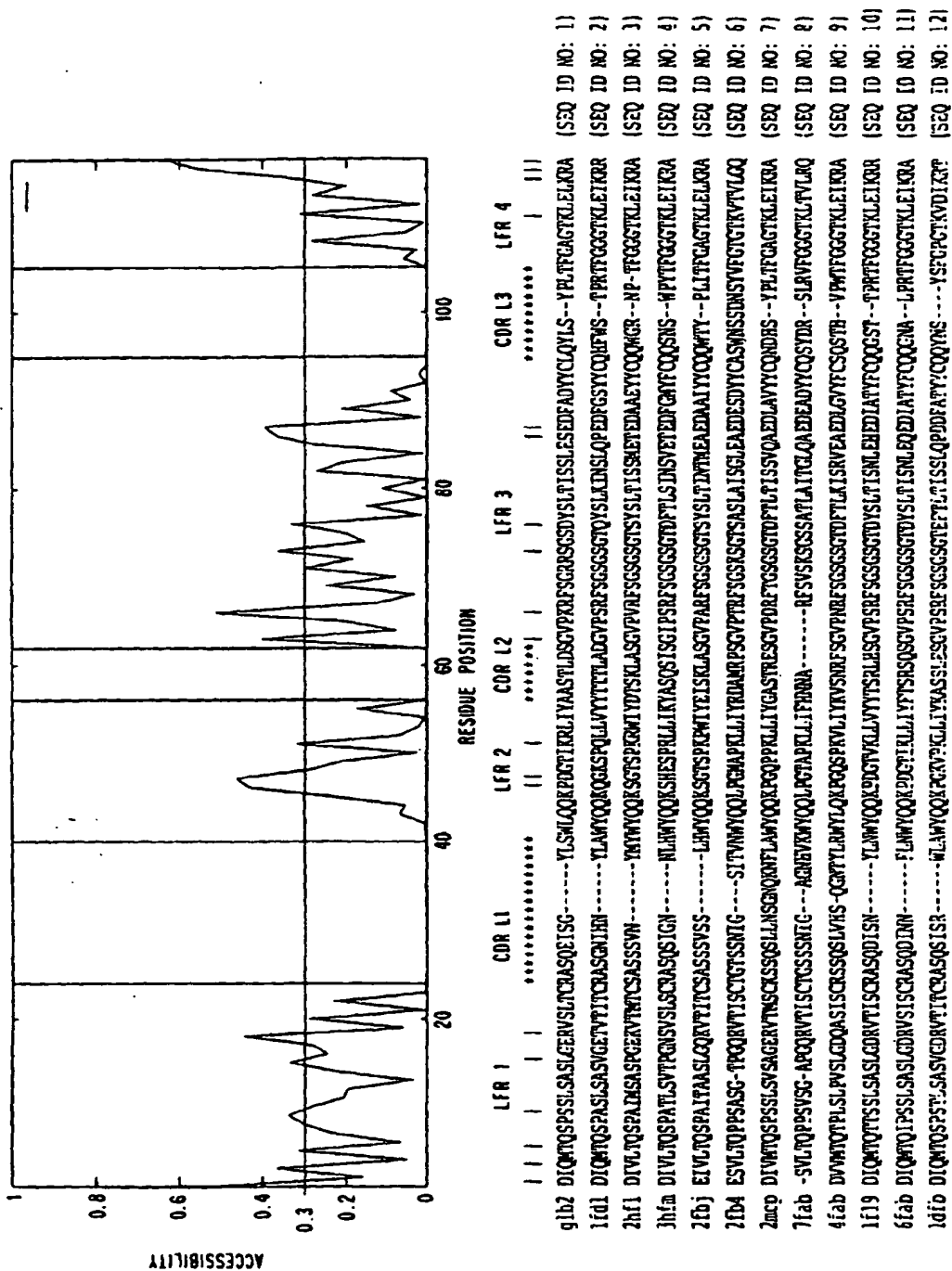


FIG. 2

FIG. 3A



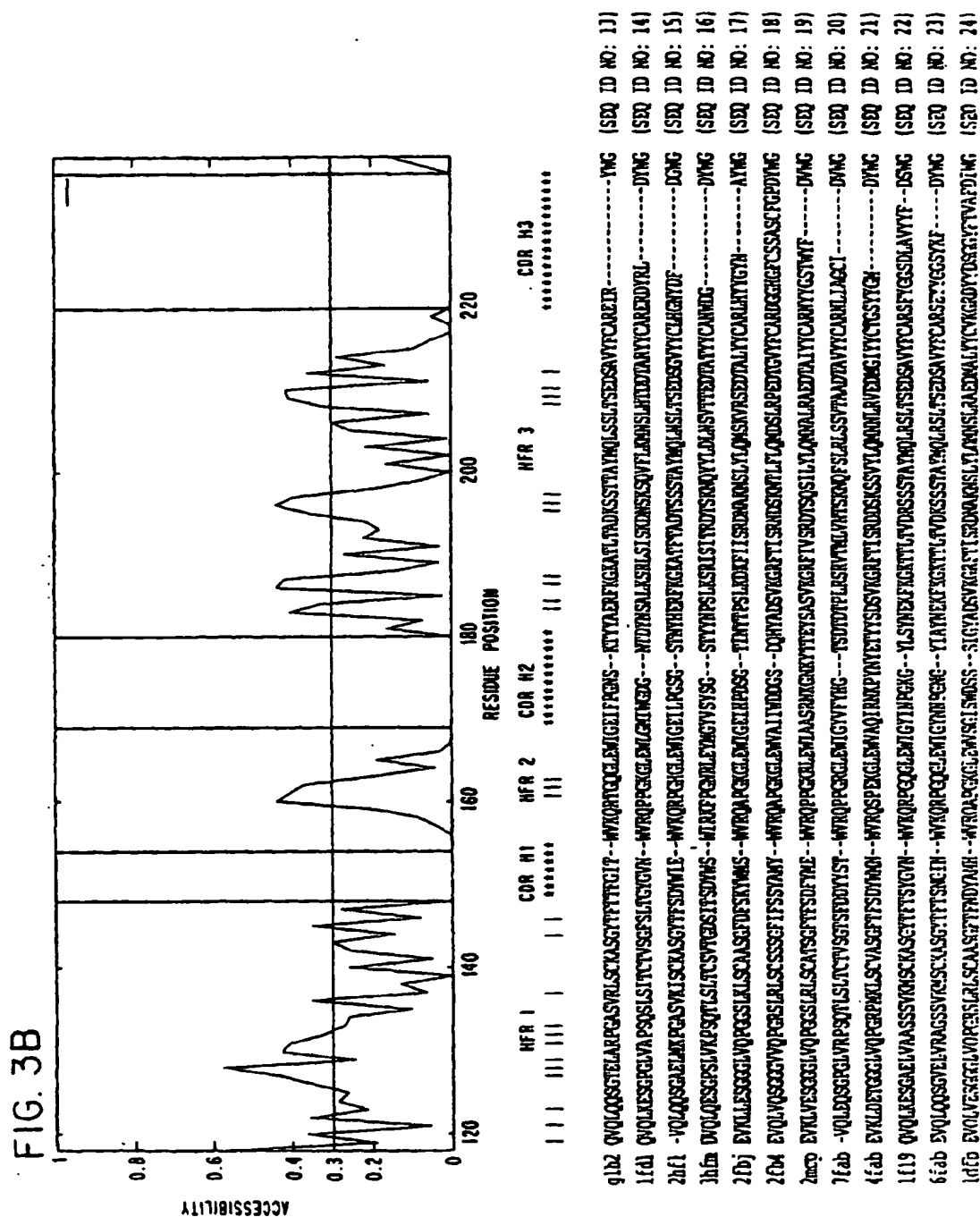


FIG. 4A

Light Chain Sequences

	10	20	30	40	50	60	70
1 N901L	DVLMTQTPLSLPVSLGQASIS	RSSQIIHSDGNTY-LE	WFLQKPGQSPKLLIY	KVSNRFS	GVPDRFSG		
2 KOL	QSVLTQPPSASG-TPGQRTISC	SGTSSNIGS----	STVN	WYQQLPGMAPKLLIY	RDAMRPS	GVPDRFSG	
3 N901L/KOL	QVLMTQTPLSPVSLGQASIS	RSSQIIHSDGNTY-LE	WFLQKPGQSPKLLIY	KVSNRFS	GVPDRFSG		
4 KV2F\$HUMAN (most identical seq)	DVMTQSPSLSPVTLGQPASIS	RSSQSLVSDGNTY-LN	WFQORPGQSPRLIY	KVSNRDS	GVPDRFSG		
5 N901L/KV2F (CDR grafted)	DVLMTQSPSLSPVTLGQPASIS	RSSQIIHSDGNTY-LE	WFQORPGQSPRLIY	KVSNRFS	GVPDRFSG		
6 KV4B\$HUMAN (most identical surf)	DIVMTQSPDSLAVSLGERATINC	KSSQSVLYSSNNKNYLA	WYQOKPGQPPKLLIY	WASTRES	GVPDRFSG		
7 N901L/KV4B (Resurfaced)	DVLMTQTPLSLPVSLGDRASIS	RSSQIIHSDGNTY-LE	WFLQKPGQSPKLLIY	KVSNRFS	GVPDRFSG		
		(L1)		(L2)			
1 N901L	SGSGTDFTLMI	SRVEAEDLG	VVYC	FGSH--VPHT	FGGCTKLEI-	(SEQ ID NO: 25)	
2 KOL	SKSGASASLAIGGLQSEDETDYYC	AAMDVSLNAYV	FGTGT	KVTVL	(44)	(SEQ ID NO: 26)	
3 N901L/KOL	SGSGTSFTLAI	SRVEAEDEG	VVYC	FGSH--VPHT	FGGCTKLEI-	(104)	(SEQ ID NO: 27)
4 KV2F\$HUMAN (most identical seq)	SGSGTDFTLKI	SRVEAEDVG	VVYC	MQGTH--WSWT	FGQGT	KVEIK	(87) (SEQ ID NO: 28)
5 N901L/KV2F (CDR grafted)	SGSGTDFTLKI	SRVEAEDVG	VVYC	FGSH--VPHT	FGGGT	KVEI-	(101) (SEQ ID NO: 29)
6 KV4B\$HUMAN (most identical surf)	SGSGTDFTLT	ISSLQAE	DVAVVYC	QQYDT---IPT	FGG	GT	KVEIK (71) (SEQ ID NO: 30)
7 N901L/KV4B (Resurfaced)	SGSGTDFTLMI	SRVEAEDLG	VVYC	FGSH--VPHT	FGGCTKLEI-	(109)	(SEQ ID NO: 31)
		(L3)					

Heavy Chain Sequences

[illegible]

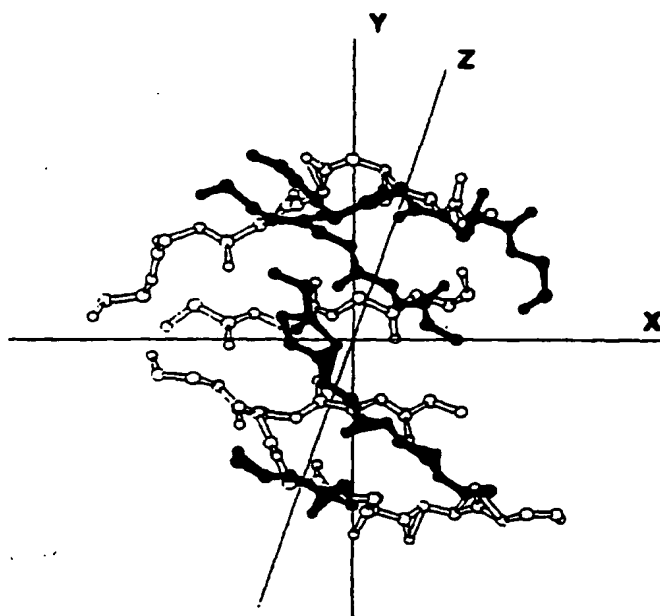
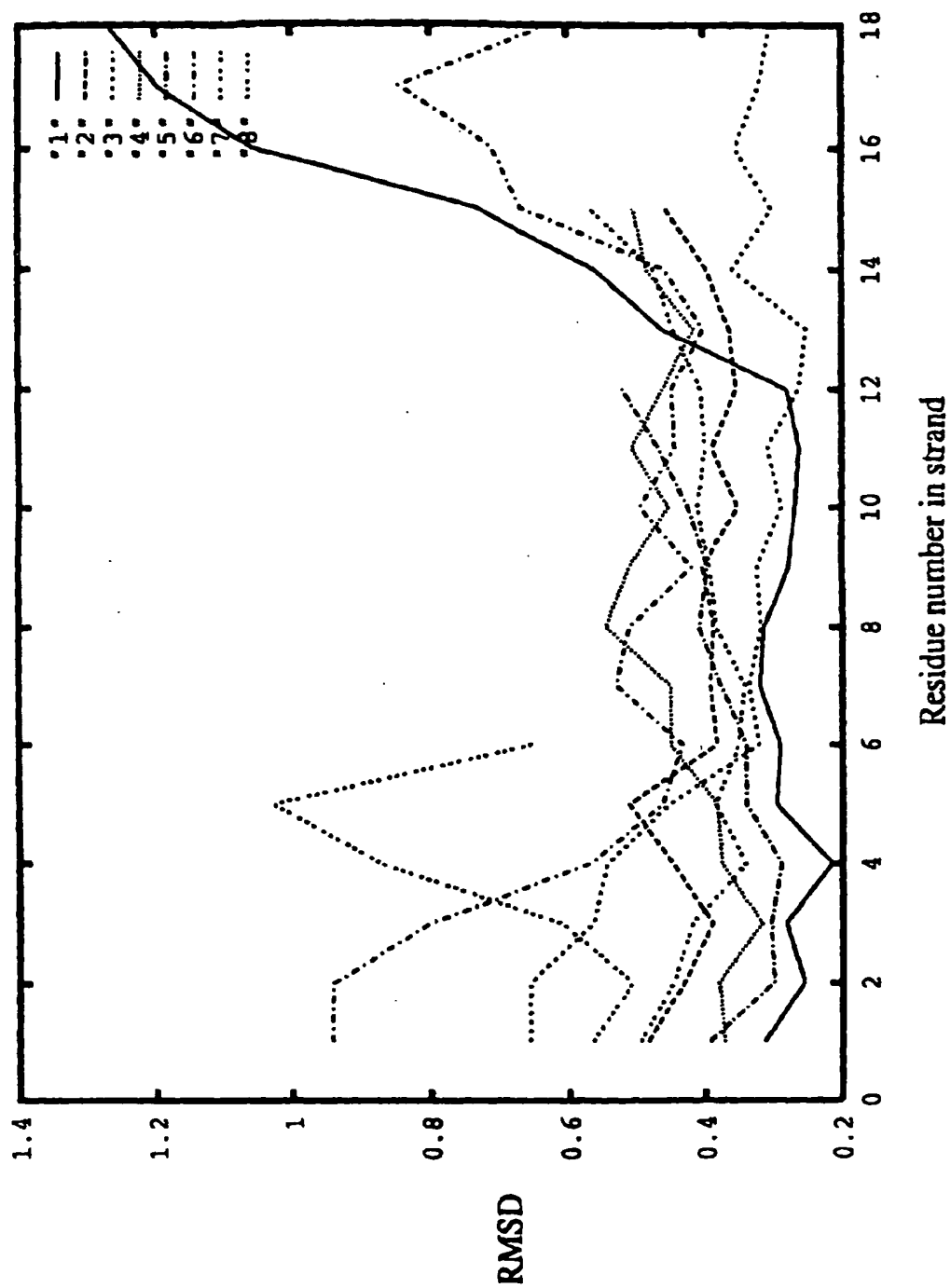
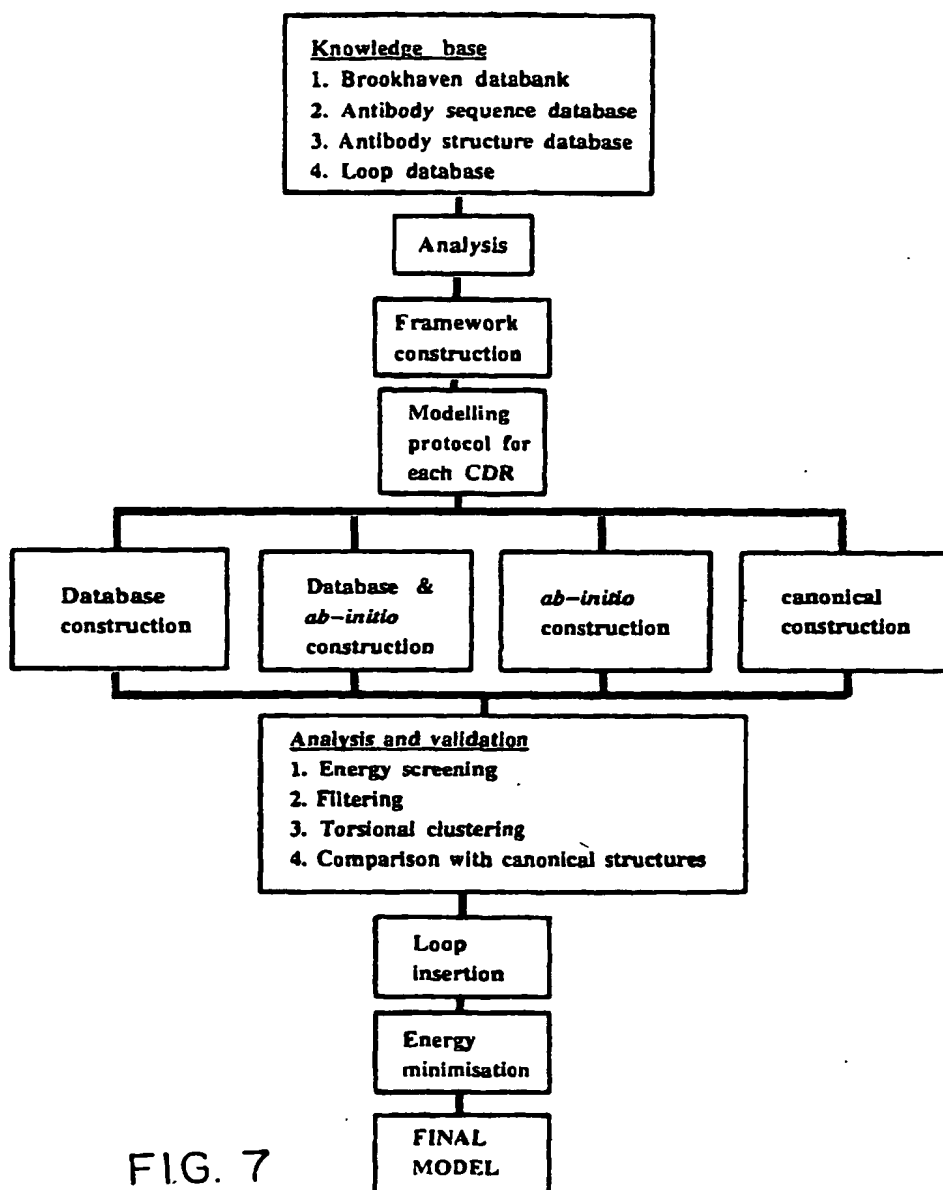


FIG. 5

FIG. 6





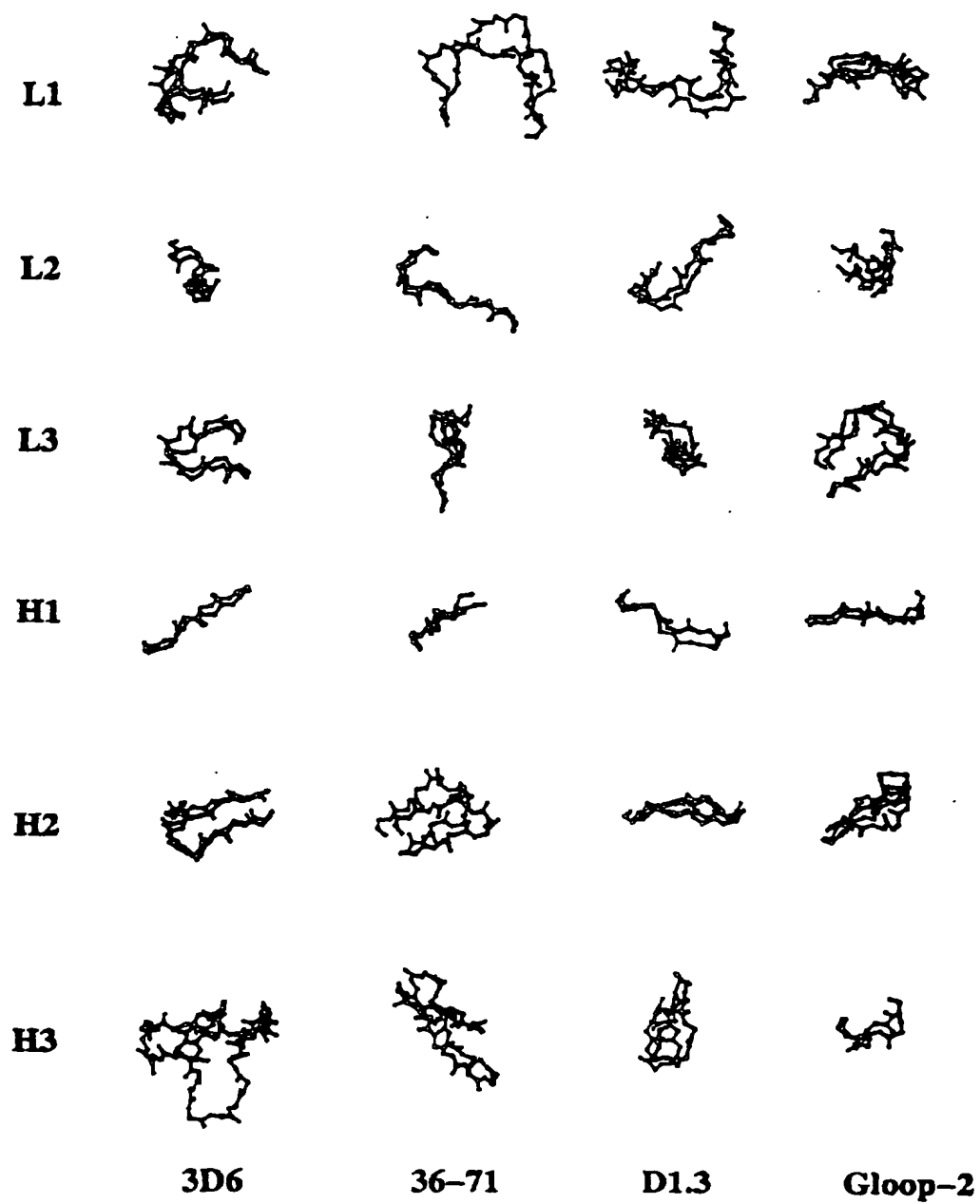


FIG. 8

FIG. 9A

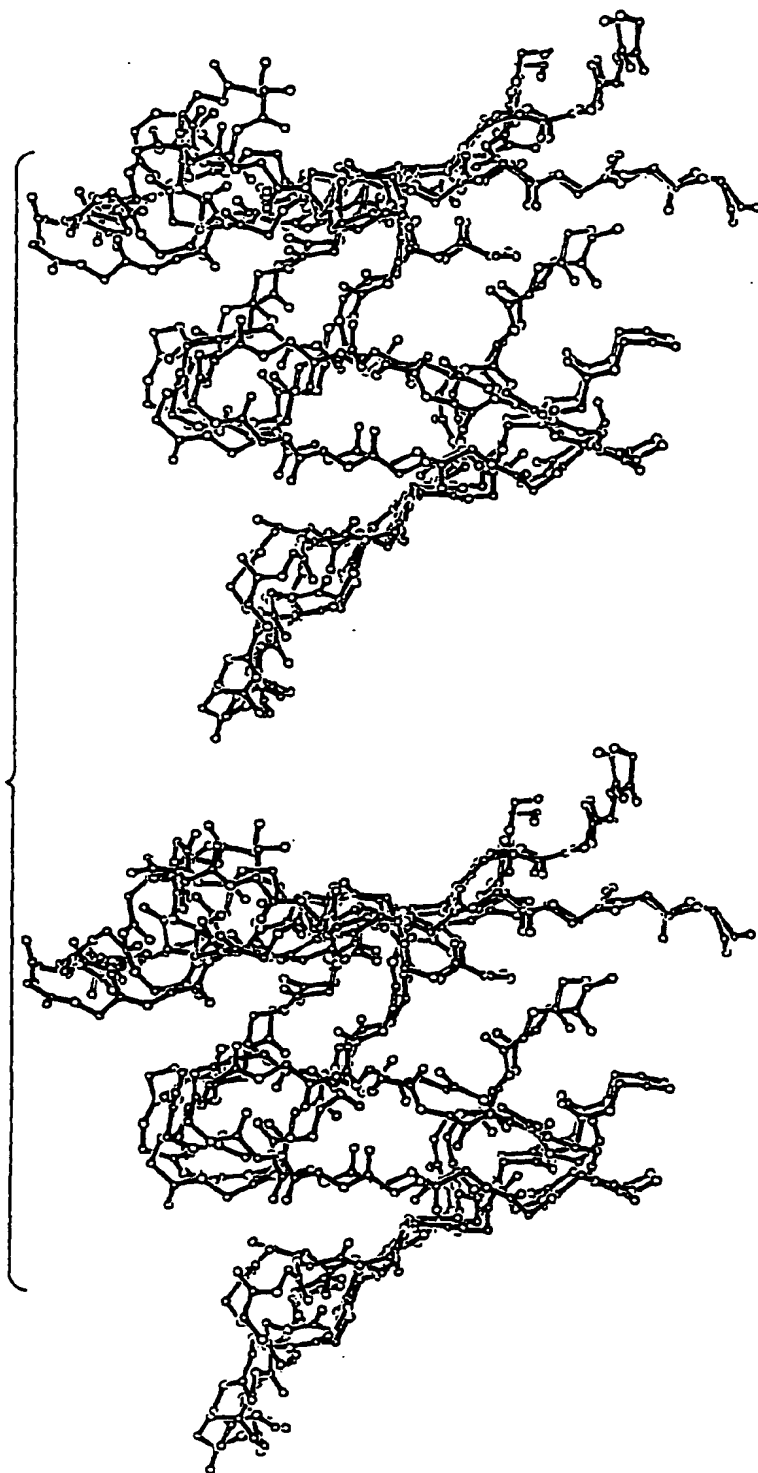


FIG. 9B

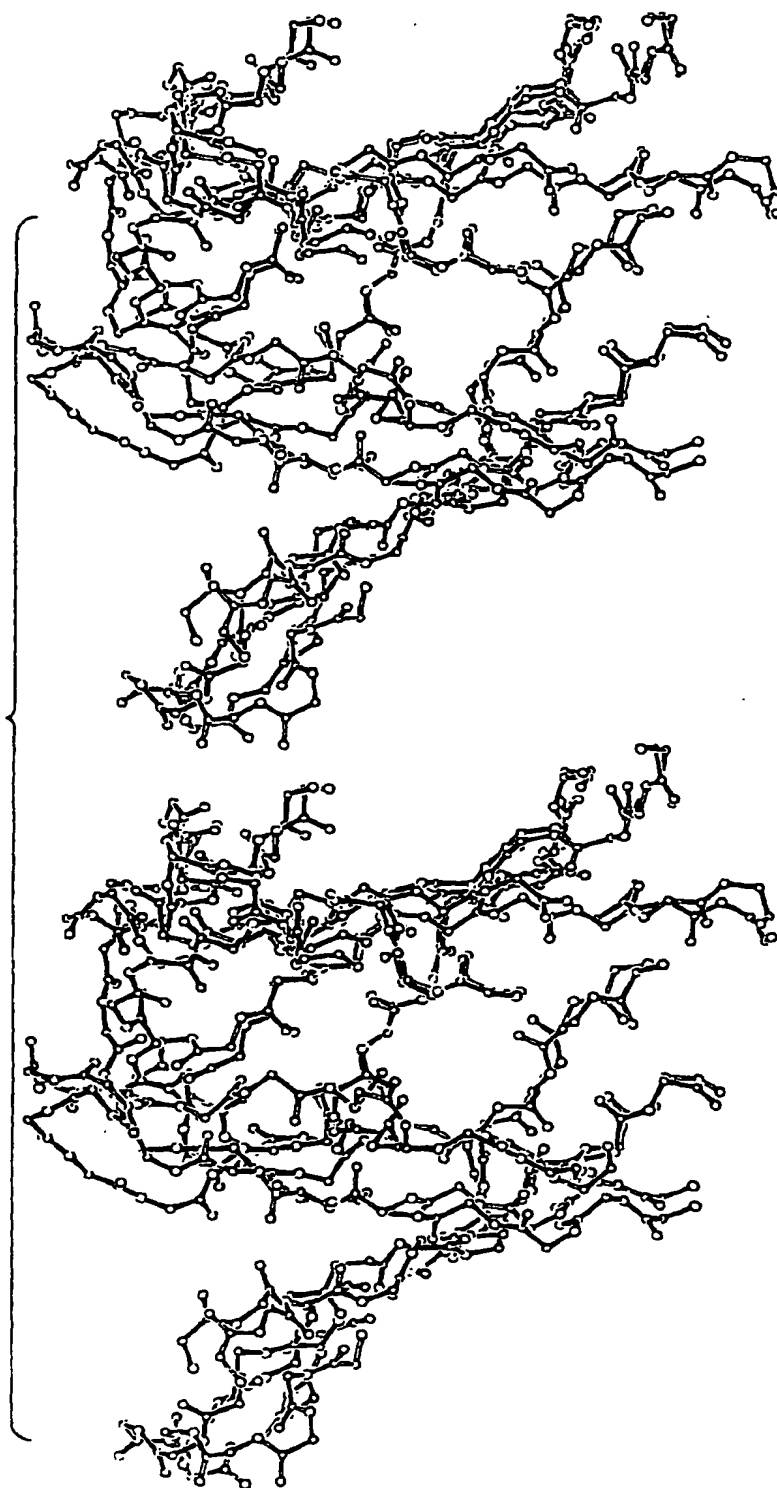


FIG. 9C

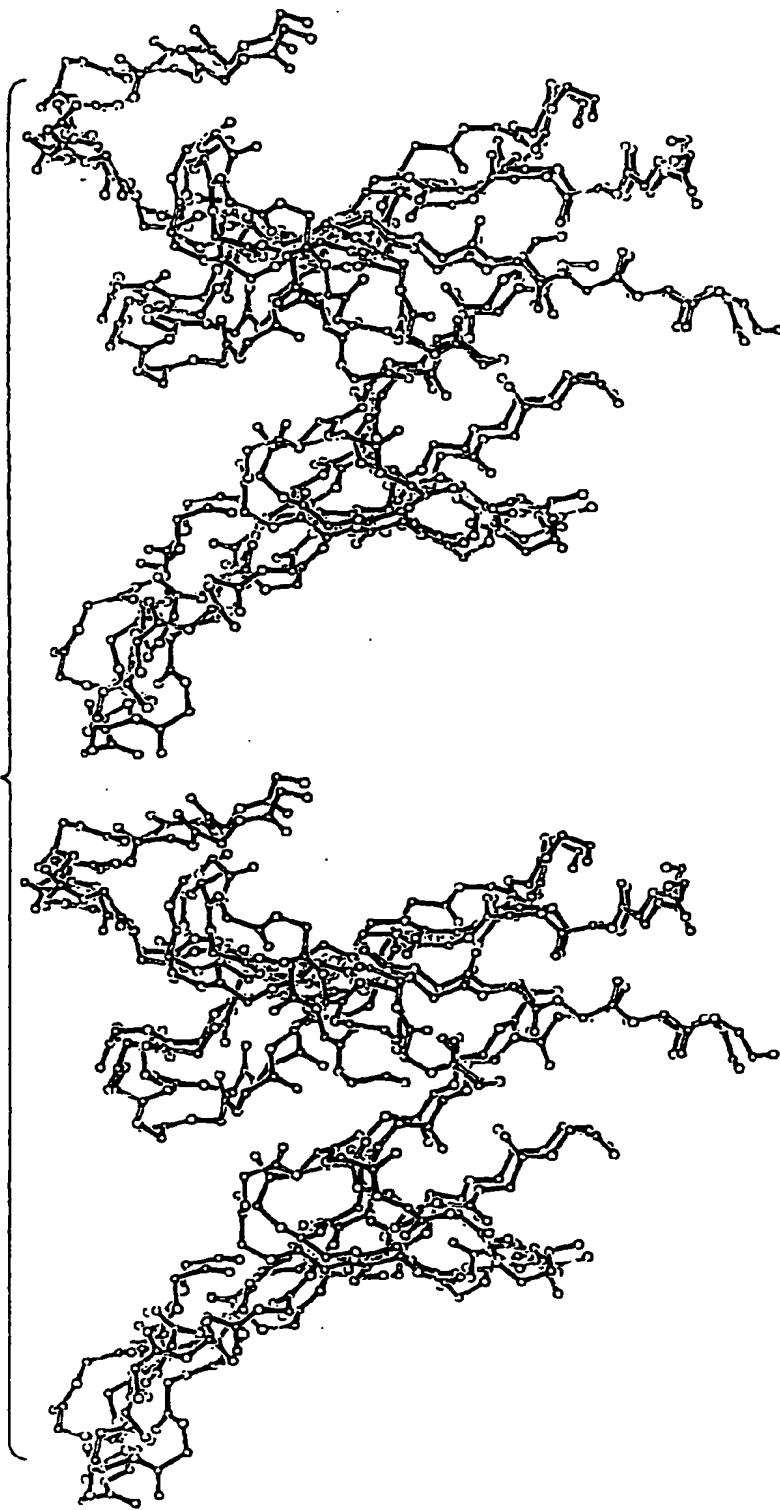
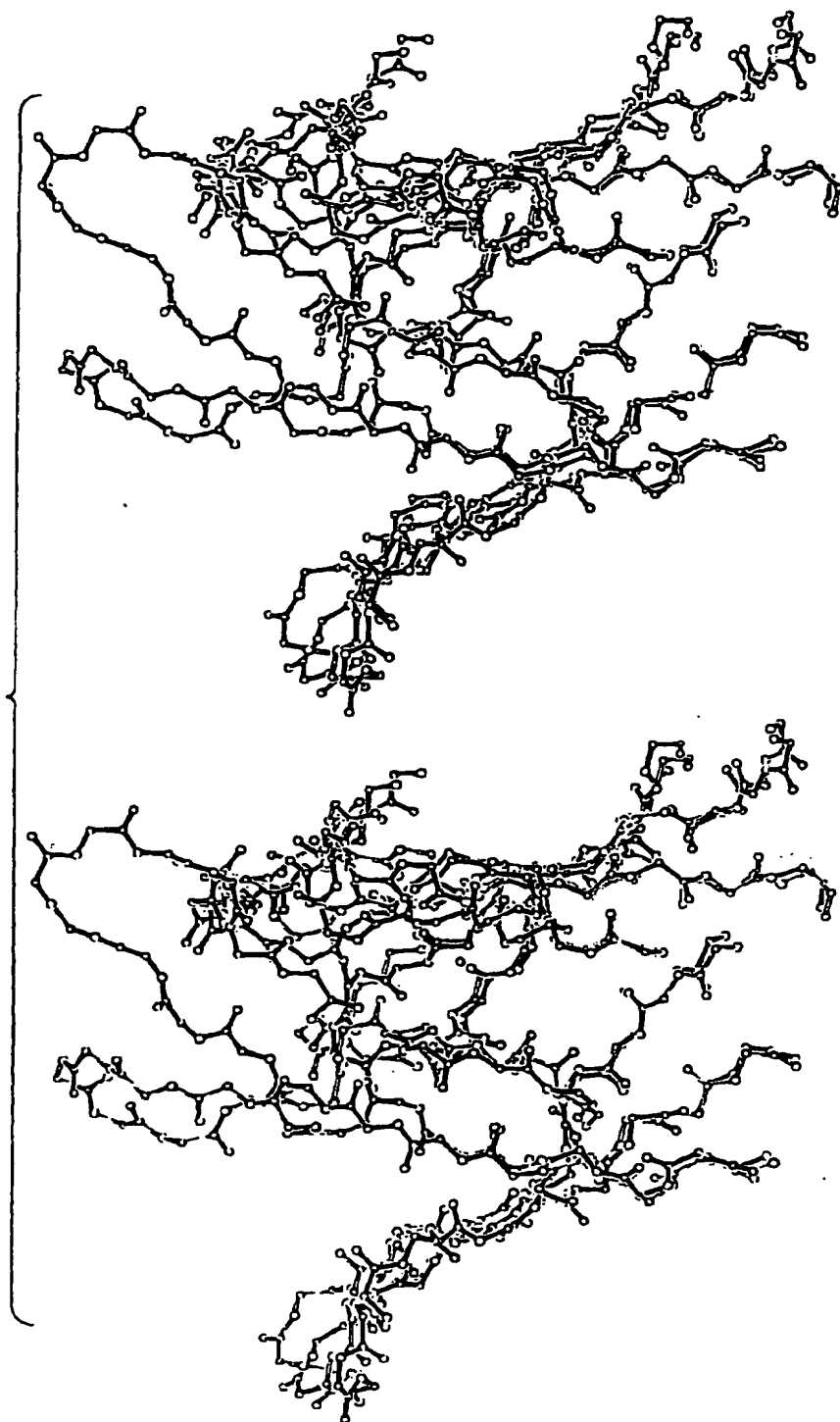


FIG. 9D



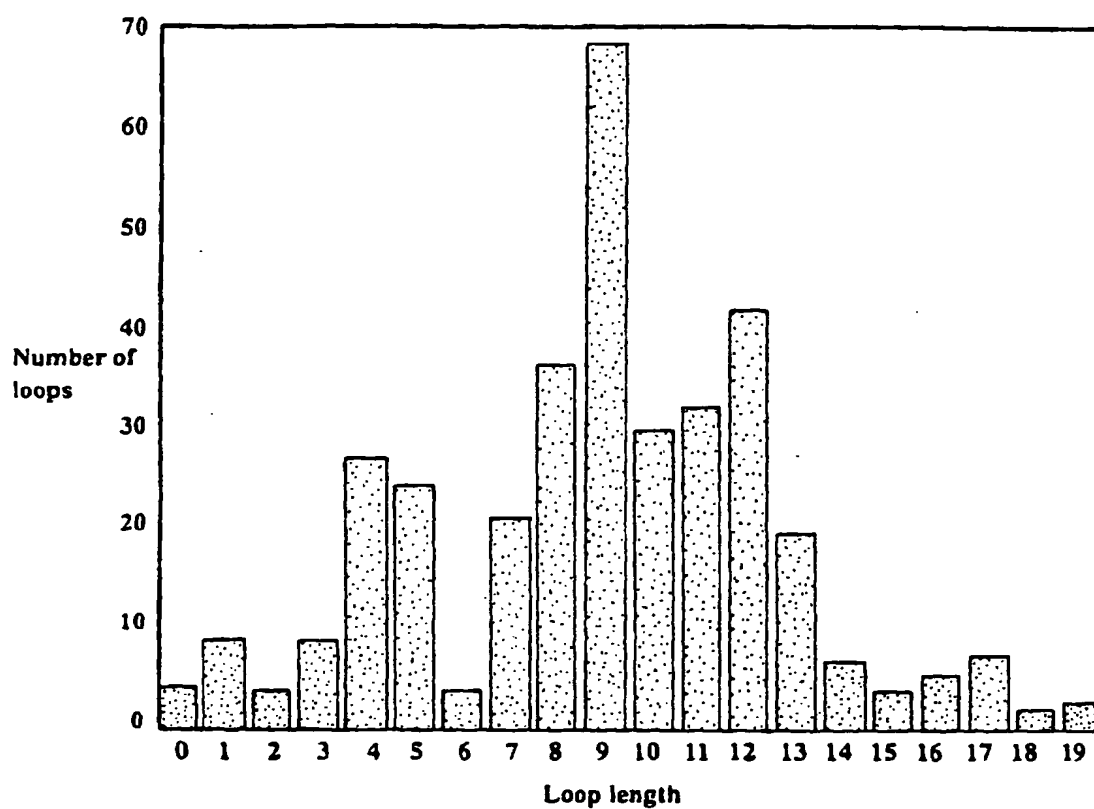


FIG. 10